The Health Impact of Chemical Exposures During the Gulf War: A Research Planning Conference

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Workgroup 3 – Treatment

Day 1 – Sunday, February 28, 1999

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. . . the session will be Monday afternoon and the workgroup will be deliberating the recommendations that they make, and also the audience will be proposing questions to the panel during the last part of that session, and during the first part of the next session, which goes over to Tuesday morning, at which time the research ideas, and really, this is not to get consensual recommendations as much as a rich amount of suggestions from which the agencies that will ultimately fund research, can dip into and utilize in making their funding decisions. So, the report will then be concluded by the group and then be presented by Dr. Natelson to the full group at the end of the conference.

There are five areas that we hope the workgroup will touch on and that members of the audience will participate in as well. We want to make sure that appropriate treatment paradigms are considered, approaches to rehabilitation, healthcare opportunities for veterans of the Gulf War, education of physicians, and appropriate study methods for treatment trials. The logistics for this afternoon are eight minutes per speaker. We ask the panel to please stay on time and identify themselves at least once or be identified by the Chair. After that, the people who are managing the audio tapes think they can recognize voices and distinguish who is who. Anybody speaking from the audience, please identify yourself, and spell your name the first time. Thanks.

Benjamin Natelson, MD, Chair
Professor, Department of Neuroscience
New Jersey Medical School
Chair: Benjamin Natelson, MD
Professor, Department of Neuroscience
New Jersey Medical School
East Orange, New Jersey

Before I go into my introductory remarks, group, the green says "parlay," the yellow says "resume." Can we just cover that up now, because I want to show you some quick overheads? I've been asked to give a very brief overview of what I want to do, and we've all been tasked by Congressman Sanders to do a lot of work, and he's here to make sure we do it, so I guess we're going to have to do it. So, here's what I'd like to do. I'd like to try and get us to agree on a number of things. Number one is in the goals. The first thing I'd like to see come out of this, and I know you do Congressman Sanders, is to increase current treatment options for veterans with Gulf War syndrome in the next one to two years. That's the short term**.** Now, since this is research oriented, we can't do this willy-nilly; we have to have a plan. So, research ways to do that, which we need to consider, is how do we assess efficacy, in such current therapeutic trials even in the doctor's office –- and we heard about one of them today, the N of 1 trial -– how do we assess the issue of compliance? Every doctor has recommended treatments and as we all know, our patients don't always follow them. Number two, an equally important thing, when our veterans are complaining they're not being heard, they're not being served, we have to be able to assess their satisfaction with what we are doing. So, this is a quality assurance issue and these are things we certainly need to do as number one. So, that's one to two years**.**

Next, we need to develop longer-term therapeutic options via controlled clinical trials. Now, I'd like to say that evidence-basing trials should have the highest priority. Ideas that are data driven. Hypothesis-based ideas without supporting data should have a lower priority because, obviously, there are a million hypotheses and only limited resources. The final question is, if we do these trials, we'd better worry about study design issues. So, these are the things that I'm going to task us to be doing.

Finally, we heard from Ed that they would like us to consider also the question of education of physicians. Here the issue is: How do you teach a doctor not to dismiss a patient just because the doctor can't hold the diagnosis in his or her hands? That is, with no lab test. And that is a critical issue because dismissing the patient is not what medicine is all about. And this is what I'd say is the crux of outpatient education because when the doctor is in the outpatient milieu, he often does not know what is wrong with the patient; he has somewhat vague complaints. And as much as medicine deals with diagnoses where you have no supportive data, for example, in my area, migraines or epilepsy, for that matter. And then finally, if we're going to educate doctors, we have to then consider how we're going to do this in a research mode, so we need to develop

ways to assess the effectiveness of our education. Did it work? Did the doctor learn? Did the doctor change his or her practice? So, these are things, again, I'd like to ask you to work on in the next few days.

Therapeutic trials. To me, a therapeutic trial is an alternative way of supporting hypotheses about cause. Most of us who do research come at it the other way. We try to find an immune abnormality, we try to find some brain abnormality. But, if you have a neat idea, and can develop a trial, you can come at it the other way and determine if your hypotheses are right. Now, that obviously requires the definition of the patient group to be studied. What is Gulf War syndrome? This workshop is not going to take on that question. I will ask you to do one of the following three things. There is a workshop worrying about "What is Gulf War syndrome." Let's defer to them. That's one option. So, don't spend much time in your deliberations worrying about that. Option number two, let's just use what Keiji Fukuda published as a case definition. It's pretty simplistic, but it worked for them. Item number three, let's use symptom-based case definitions that are out there already -- CFS, fibromyalgia, MCS – they're all there, we all know how to define them, or we certainly can quickly settle that, not here, but in the hallway. Therapeutic trials require hypotheses as the cause. Again, evidence-based hypotheses have to be preferred. Without data, any hypothesis is possible and, obviously, testing every idea is not possible. There are not the resources to do that. How can we achieve the goals in these four meetings and try to come up with short-term goals? Mr. Sanders says, "I want something now," and longer-term goals, that we can develop treatment trials that are outside of the box.

Well, I tried to help us come up with an idea, it's my idea. I think that we need to make a decision amongst ourselves as to what each of us wants to do. And I have come up with four different treatment modalities that I think encompass everything, and I want everyone to sort of pick the one that he or she wants to focus on. Let me just go through this quickly.

Rehab medicine approaches. What is the rehab medicine approach? It is non-pharmacological, by definition. So, examples of rehab medicine approaches that are not currently being tested on Gulf veterans with Gulf War syndrome might be, I'm just making these up, acupuncture or breathing exercises. Those are Rehab medicine approaches.

Then there are pharmacological approaches. Examples are low-dose tricyclic anti-depressants to relieve pain and sleep disturbances. That's what I do with any patient with chronic fatigue syndrome or fibromyalgia. It's based on trials in those illnesses occurring in different demographic groups. Maybe they need to be tried in Gulf veterans with those illnesses.

Psychological approaches. One such approach might be eye movement desensitization, for uncomplicated PTSD. That's an individual who has Gulf War syndrome and PTSD. Let's try to remove the PTSD. From what I understand, I'm not a psychiatrist, that's an ailment that's very hard to treat. There's an experimental treatment that I've recently heard about and read a little

about that looks pretty interesting.

And then there's the fourth group, Other. An example of other is to treat self-reported food allergies with restriction diets to see whether these work, and then perhaps probe the individual with one trial with the offending food.

So, what I would like to ask the panel to do is to please pick one the above with the following in mind. My idea is if you pick one of the above, then our job is not so gargantuan. All of us don't have to worry about coming up with the short and longer-term solutions. I can come up with the short and longer-term solutions maybe for the drugs and one of you can do one of the other modalities that I've laid out.

So, just to finish, let's go again, work on therapeutic ideas which are not about to be tested on Gulf vets with Gulf War syndrome. What's that mean? Well sure, we can discuss cognitive behavioral therapy, and we should up here, but as a jumping-off point, why focus on it? Well, the Veterans' Affairs Department plans to test its efficacy in a large trial that two of our panelists have designed. So, that's already fortunately in the hopper. So what we need to do then, is to try to develop a better, or the next, potential therapy because that's already cooking. Drug trial examples. This is something that I've thought a little bit about. There are drug trials out there right now. The UK group published a paper two weeks ago in *The Lancet* on "low-dose cortisol in chronic fatigue syndrome." Is chronic fatigue syndrome in veterans, a demographically different group in terms of gender, background race, etc., etc., going to respond to low-dose cortisol? If so, should we do a longer trial than was in the *Lancet* paper? Ampligen is an immunologically-active drug which a drug company has out there right now, which has been approved by the FDA to do a large double-blind, placebo-controlled trial of infusion. One very simple thing we can do is encourage veterans who fulfill the case definition for CFS to participate in that trial. That will then determine whether the veteran has an immunological cause. Modafinil, a brand new drug, released for narcolepsy, excessive daytime sleepiness, no one, to my knowledge, has tried this on any fatiguing illness. So, that may be an appropriate trial. And then last, a trial that has just been completed that I know about in the United States, using a cholimomimetic agent called galantamine, again in chronic fatigue syndrome, well galantamine is not available, but there are cholinomimetics used in cognitive disorders which could be tried**.**

So, there's my little shopping list of some things that we can do right away. So without further ado, I'm hoping that each of you will choose one and if all of you have chosen one and I'm the only one to be in the other, well, we'll have to figure it out. Now it's time for our eight-minute talks, and I'm going to start. So if we can put the first slide on, I'm going to quickly go through what we found when we did an exercise trial in chronic fatigue syndrome because no one on this side of the Atlantic has tried, has looked at a controlled exercise trial, and our questions were:

‘ Would CFS patients benefit?

- Will the exercise change any of the symptoms?

- Will aerobic exercise training change overall fitness?

- Will patients with CFS resemble healthy sedentary people following training?

So, that's the logic. We studied 21 CFS patients whom we trained, 17 whom we didn't, our controls were healthy sedentary patients and you see we had trained and untrained. Basically, what we did is a graded maximal treadmill test. There you go as far as you can, to determine the parameters for training, and then we did submaximal training beginning with ten minute bouts three time a week for ten weeks. We chose a very mild initial workload.

Obviously, the individual had to be able to walk for ten minutes. We increased it to twenty minutes, and then we increased the workload. If you look at the next slide, this basically shows you in terms of maximal effort that one could make, we started with 40%, we ended with 60%, we began with ten minutes on the treadmill and at the end of the tenth week, with twenty minutes. Next slide. These then are the change in the amount of time the individual could exercise. These are the untrained people. You can see that after ten weeks, they weren't trained, so they could walk just about the same amount of time. These are box plots that give you some sense of variability, but just sort of focus on the middle. The point is that both the CFS and the controlled had a small amount of increase, rather small, but significant.

Next slide. Here we're looking at the minor CFS symptoms, and these are untrained people, and we were able to reduce the symptoms in the CFS patients significantly. Next slide. But we were not able to alter the fatigue. This is a multi-dimensional fatigue inventory. No change really in any of our subjects, whether they were trained or untrained.

So the last slide is: What do we conclude? One thing that our patients were very worried about was that they couldn't even do any exercise. We now know that they can participate in exercise trial without harm. The results are reduced symptoms and improved capacity, but fatigue remains unchanged. Therefore, this treatment is amelioratory and not curative. That means, in our hands, and this was a careful trial with a physical therapy assistant, a training assistant, CFS remains, so we conclude that exercise should be part of the therapeutic regimen, but obviously, cost-benefit questions remain. No one is going to do it with a physical therapy assistant. They'll have to do exercise in a less costly way. So, I'd like to ask then the next speaker, Becky Bascom, if you'd like to present.

Rebecca Bascom, MD, MPH
Professor of Medicine
Pennsylvania State College of Medicine

Hershey, Pennsylvania

I'm primarily interested in having an instrument to use in treatment trials that bridges the gap between science and the suffering of individual veterans. What do I mean by that? Well, in the American Thoracic Society currently, we're working on a document called *Guidelines as to What Constitutes an Adverse Health Effect*. It's something that's been used a lot for air pollution setting standards. Twenty years ago, we said that an adverse health effect would be defined by a measure of lung function. If your FEV_1 went down, for example, and that's how we should decide if something is adverse. Since that time, many people have noticed that what's important to patients is maybe not being addressed. And I think Ben's very nice study is an example of that, because he looked at time to exercise and concluded that, yes, there was conditioning and, no, there was not fatigue.

But what he didn't have is an instrument that said, "What's important to the chronic fatigue patient?" And an aggregate. What makes them feel bad? And not just their fatigue, but how about whether or not they can go out at night, or whether or not they can last until supper time? There is now a discipline that goes by the common name of quality of life. So, people have developed quality of life instruments for a whole variety of conditions. Liz Juniper up in Canada has done it for asthma and allergic rhinitis, and it has been characterized so well that the Food and Drug Administration is now willing to accept quality of life outcomes as evidence of efficacy when they are considering a medication. Quality of life instruments are much more than, "Gee, how do you feel?" But, they were developed by listening to the patient and having the patient say what's important.

One example to illustrate this is for kids and allergic rhinitis. Liz started off talking to the parents to figure out what was important to the quality of life of a kid with allergic rhinitis. And the parents said, "Well, obviously, it's when that green stuff is coming out of their nose. That's the most adverse effect you can imagine." So, the parents would rate that very high. It turned out, if you talked to the kids, they didn't really care about that. What they cared about was how stuffy their nose was, and how hard it was to take in a breath, and whether or not they could run on a playground with their friends, and whether or not they'd wake up at night.

So, by actually asking the people who you are trying to intervene with, who you are trying to find something to help, and have them work with these quality of life people, to have them come up with a quality of life instrument, I think would be very powerful in helping us know whether we're making any progress. This is particularly important because we do not have a specific biomarker. There are a hundred different treatments, there are a hundred different tests, but there is a consistency to the story people tell and that rings true with the patients that I've seen over the years. So my specific recommendation, Dr. Chairman, is that one key, early initiative is that a quality of life instrument be developed and validated that can be used as an outcome measure for all of these treatment studies.

Dr. Benjamin Natelson, Chair

Thank you very much. Stuart Brooks, do you want to say something?

Stuart Brooks, MD
Professor, Colleges of Medicine and Public Health
Director, Sunshine Education and Research Center
Department of Environmental Health & Occupational Health
University of South Florida
Tampa, Florida

Thank you. Just a few words. I think it's important, with a lot of disagreement on etiology and a lot of the questions dealing with mechanisms, that we really try and address the problems. And I think that we should attempt to identify treatment protocols that can be used currently without really worrying about what the cause is, at least at this point. I think the field, as I see it, is so controversial, and perhaps very difficult to identify specific etiologic factors, that I think we need to really address treatment protocols. And I think there are a variety of treatment protocols. Some of those have been mentioned that can be attempted and can be tried – some of the cognitive therapy that will be discussed, some of the wellness protocols, some of the things that you suggested, exercise programs, and a variety of other programs that could be tried and attempted without really dealing with trying to argue or trying to reach a specific etiology. This may be, as we have mentioned, a complex process where there are a lot of different causes, so trying to find one cause is not going to be the answer, and as was mentioned by the veterans today, and what seems to be the emphasis, is that they're interested in treatment, and I think that would be the primary goal. Try to identify and test various treatment protocols and try to put them into use as soon as possible.

Dr. Benjamin Natelson, Chair

Thank you. Dan Clauw.

Dan Clauw, MD
Associate Professor of Medicine and Orthopedics
Chief, Division of Rheumatology, Immunology, and Allergy
Georgetown University
Washington, DC

I'd like to begin by saying that I don't think we have very good science to guide us in this regard, and I feel a little bit uncomfortable as a scientist talking about primarily anecdotes. But, I think that's what we're left with, and that's how we need to move forward from this point. So, most of what I'm going to talk about is anecdotal. I think the only science that we have to guide us in to

how to treat, in particular, the subset of individuals with multiple chemical sensitivity, is perhaps the randomized controlled trials that are done in similar illnesses such as fibromyalgia and chronic fatigue syndrome. That's certainly the science that we used when we tried to put together the big VA cooperative trials that are looking at things like aerobic exercise and cognitive behavioral therapy. That since those types of treatments worked in illnesses like fibromyalgia and chronic fatigue syndrome, that it would make sense that they should work in closely-related illnesses like multiple chemical sensitivity and/or illnesses such as Gulf War illnesses.

My feeling is though, that when I take care of patients clinically, and again I'm putting on a different hat, a clinician hat, an anecdotal hat, not a scientific hat, that there are a couple of things that I feel strongly about. One is that I think that we can divide these illnesses into two main parts. One is the underlying physiology of the illness, which we don't understand very well, but I think most of us are beginning to feel comfortable that this is some kind of dysfunction involving the central nervous system, there are abnormalities in how people process sensory information and there are abnormalities in things such as autonomic function that characterize subsets of patients with this illness. And I think the other big component of this illness is the kind of consequences that occur as a result of this illness. People with this illness, once they become symptomatic, develop a number of problems including deconditioning, including loss of their function in different aspects of their life, including concurrent mood disorders. And I think if you are treating individuals with this spectrum of illness, if you try to treat the physiology and you don't understand the consequences, you'll get very little, and if you just try to treat the consequences and don't try to address the underlying physiology, you don't get very far.

My own feeling, clinically, is what I do, is first try to find a symptom-based medication that can make people feel better and I think that after you do that, the other types of interventions like aerobic exercise and cognitive behavioral therapy are much more effective. People are much more likely to adhere to these treatments. They're much more likely to tolerate these treatments when they're not in such severe pain, when they're not having such severe chemical sensitivity and when their fatigue level is such that they can actually do exercise. My feeling, likewise, is that there are a couple of classes of medications that have been well-studied in this spectrum of illness. Ben already mentioned one of them that I think could very easily be used in a randomized control trial, or better yet, an N of 1 trial, and that is low doses of tricyclic drugs. If you look through the entire spectrum of illness, migraine headaches, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, the tricyclic drugs have been tested and shown to be effective in most of the illnesses within this spectrum. And again**,** from a clinical standpoint, there's only one tricyclic drug that I find people with multiple chemical sensitivity can tolerate, and it's called doxepin, because it's the only one that comes in a liquid suspension and it can be started in a dose that's low enough for people to tolerate that have chemical sensitivity. All the other tricyclic drugs, if you try to start at the initial dose of the tablet, it's way too high and people don't tolerate it. But I have a lot of people on extremely low doses of doxepin – three or four drops of doxepin, which is one milligram or two milligrams. It may take them a week or months to get to that dose, but

they seem in some way to be helped from a standpoint of underlying physiology, even on those tiny doses of these tricyclic drugs.

The other class, if we're going to do an N of 1 trial, and if we're going to acknowledge that what we need to do in these treatment trials is to develop three or four different medications that people might respond to and use them serially, that's what N of 1 trials really are, that perhaps another class of medications that I would suggest are low doses of beta blockers. Again beta blockers are targeting the effector mechanism in this spectrum of illness, that is, the autonomic nervous system. Very low doses of drugs like Inderal, again, seem to help subsets of people with this illness improve subsets of symptoms that they have with these illnesses.

So, my suggestions, to sort of sum up, would be to consider doing N of 1 trials where you very clearly lay out that each individual will receive a series of drugs starting at very tiny dosages and slowly escalating the dose of the drug until the person has symptomatic improvement, or until they don't tolerate the medication which is going to be a problem in a number of individuals, in particular, those that have the MCS component. But that if we do these trials, we'll learn an awful lot about subsets of individuals with these illnesses as well as what treatments would be effective in larger numbers of people with these illnesses. And then, once people get improvement from some type of symptom-based pharmacotherapy, I think the behavioral interventions, the aerobic exercise and the things that are really addressing more the consequences of the illness rather than the primary physiologic cause, are likely to be more effective. Thanks.

Dr. Benjamin Natelson, Chair

Very good. Our next speaker is Chuck Engel.

LTC Charles C. Engel, Jr., MD, MPH
Chief, Gulf War Health Center
Walter Reed Army Medical Center
Washington, DC

Thank you. Just by way of introduction, I guess my perspective on the symptoms that Gulf War veterans seem to be experiencing, are experiencing, is affected by multiple perspectives that I have. One is as a Gulf War veteran myself. As a Gulf War veteran, I am personally bothered by the suffering that I see a lot of people who shared a similar experience to mine, are very obviously going through. And, research has shown that their experience is a consequence of Gulf War service. Another perspective that I have is that of the clinician, one who has tried for a number of years, even pre-dating the Gulf War, to assist in whatever way that we can, people who have medically poorly explained physical symptoms and looking for strategies to help them because as a clinician I'm aware that this is a frustrating and vexing problem and not one that's taken care of in the usual ten minute visit. I also bring the perspective of an epidemiologist who has done grant

funded research and published from those projects, in that I would like to see that whatever we do is evidence-based. I think that we don't have to rely solely on anecdotes, that there are evidence-based treatments that are available out there that have been applied to analogous populations of folks with physical symptom-based disorders and I am interested in exploring how effective those modalities are when used for Gulf War veterans.

Along the latter lines, my job for the last 2 ½ years has been to work with Gulf War veterans that are ill as the Chief of the Gulf War Health Center where we have a 3-week multi-disciplinary intervention that we provide for them, which is really rehab in orientation, ameliorative toward suffering. Although I say non-pharmacologic, certainly medications are part of it, because many of these patients are already on a multitude of medications. The patient population, as I define it, is sort of a pragmatic definition, that is, those folks who when they come to see the doctor, they tell the doctor about a myriad of physical symptoms in many cases, relating sensitivities and so on, that on examination and medical testing that the doctor comes up empty-handed. That is not to diminish the veterans' experience, but what unfortunately does happen in many cases in healthcare, is that given that set of medical data, the clinician does feel disarmed and unhelpful and sometimes diminishes the patients' experiences as a result.

Folks with these physical symptom-based disorders, representing about 1/3 or 1/4 of the population seen in the average primary care setting, I think that there's a lot we could learn by looking at interventions that could be brought to primary care settings as well as in more intensive specialty settings that are more rehab in nature. The sort of intervention that we use involves what I would describe as three basic modalities. One is collaboration – that it involves collaboration among disciplines and it also, and probably more importantly, involves collaboration between the veteran and the healthcare provider. I think over the history of healthcare, what has evolved in the social arena, is a very powerful physician and a less than powerful patient who comes in and the physician tells them what to do for their symptoms, often in the setting of a ten minute visit, in which case the usual recommendation is, "Take a pill." I think that healthcare requires greater interpersonal attention than that and what we have attempted to do is create a collaborative dialogue with veterans where they tell us what they feel is wrong, we learn from them about the impact of that on their lives. We find that there's widely divergent stories in their regard, and from that we work with them in whatever way we can to ameliorate the situations that they have that are causing disability.

The second element of the program is really aimed towards disability itself. It targets disability rather than a disease, and that element is a program of supervised and gradual exercise, the sort of thing that has been used for chronic fatigue syndrome patients and fibromyalgia patients in the past.

The third part, in keeping with the collaborative model, is to help patients learn about their conditions and maybe more importantly again, to help their significant others learn about their

health conditions – what's known about co-existing medical conditions what we do know that they don't have, based on biomedical work up, how to work best with physicians and active strategies for improving function rather than more passive strategies such as waiting on doctors to come up with answers through a myriad of diagnostic testing.

The outcomes of interest that we have focused on are improving health, rather than specifically, a narrow set of symptoms, overall quality of life, diminishing patients' distress about their health, diminishing physical symptoms as well, although less down the list. What we have seen so far is promising. We have not performed a controlled study to date. We are doing comparisons of baseline versus subsequent comparisons. We have 3-month data at this point in time which shows modest but global improvement in quality of life and distress as well as physical health concerns, and to some degree in symptomatology. And most notably in symptomatology we found that looking back on their history of symptoms in the six months prior to the program, symptoms had been increasing gradually, and subsequent to their participation in our 3-week outpatient program, that they have noted a modest decline in physical symptoms. Not a cure, but definitely an improvement.

So, I am interested in looking at ways in which we can adapt modalities such as that, which are, most of the components of our program are evidence-based, and I'm interested in adapting various modalities that have been looked at perhaps one at a time in a sort of multi-faceted approach to Gulf War veterans' chronic physical symptoms.

Dr. Benjamin Natelson, Chair

Thanks, that's good. Let me tell the audience, the reason I haven't asked us to identify ourselves and tell you about us, is because you have these brief bios which you can look at to identify who's speaking. Next, Nancy Fiedler.

Nancy Fiedler, PhD
Associate Professor
Department of Environmental and Community Medicine
UMDNJ-Robert Wood Johnson Medical School
Piscataway, New Jersey

I was very glad you used the word "collaborative." I'd written it down about two seconds before you said it. I'm going to focus my remarks probably more on chemical sensitivity because of my experience in treating patients both with chemical sensitivity, and also patients who have been exposed occupationally to chemicals and don't get "better" under the rules of toxicology.

But I want to back up, because I realize that we do need to put this in a context of evaluation of

treatment protocols. So, I think it's very important first of all that we have to consider how we are going to enter people in these treatment trials in terms of the interventions we might use. And that fits into what I consider to be points of intervention that may be useful in my trial and error efforts with patients. I find that it is very important first of all to put people in categories based on problem focus. Now, that problem focus may be a particular symptom complex, or it may be a group of chemicals or products that cause them more problems than another. But, in certainly the psycho-therapeutic literature, we've used that behavioral focus for a long time in identifying those kinds of problems and prioritizing, "What are the most troublesome symptoms, what are the most troublesome chemicals to you?" That would then follow in terms of the kind of interventions that can be conducted.

In terms of intervention, I don't think we have an answer to etiology, and I think there's going to be more than one area of etiology in most of the symptoms. Then I think the interventions have to be what I call multi-modal, and what that means is that it isn't going to just be exercise, or drug therapy, or possibly cognitive behavioral therapy, but rather a combination of those for patients. This may suggest we need single case design studies, and there's a large literature on single case design studies that can be called upon to look at various multi-modal treatments to address patients. For example, some patients in my practice have been able to tolerate being in public and being around chemical exposures, and they've been able to tolerate it because we've identified that component of their response that's anxiety. That doesn't mean anxiety causes their response, that means it exacerbates their response. And when we treat that with a combination of relaxation treatment and behavioral methods, they can then be around chemicals enough to be able to function in the world and continue to be employed rather than unemployed.

So again, these are problem-focused, problem-solving approaches as opposed to a diagnostic, and then you treat everyone in that diagnosis with one particular kind of intervention. And again, I think that avoidance may be one aspect of treatment and there may be certain factors that have to be avoided because a person cannot tolerate those at all. So, I think that what I am calling for is something that crosses over the categories that Ben gave in terms of rehabilitation medicine, low dose medications, psycho-therapeutic interventions and even in terms of avoidance, say of certain foods and chemicals, because I think each one of these has a contribution to make to the illnesses presented by Gulf War veterans, and we have to first assess what the primary problems are, put people in groups according to those primary problems, gear our interventions towards those problems, and evaluate them. And I think Becky made a very good point about quality of life even being incorporated into cancer treatment these days in terms of what kinds of interventions we use as being an important outcome.

Dr. Benjamin Natelson, Chair

Thank you. Dr. Gordon.

Victor Gordan, MD
Staff Physician, Outpatient Services
Manchester VA Medical Center
Manchester, New Hampshire

I will concentrate my presentation on the observation which I gathered from evaluating over 650 Persian Gulf veterans at the VA hospital in Manchester, New Hampshire. I have had an observation for years and years that the standard treatment which we offer to the veterans, and I do offer the same treatment as everybody else in this country, treating individual symptoms for relief of symptoms is very disappointing. Some of the symptoms I cannot treat, and nobody on this earth has the knowledge of how to treat the symptoms like fatigue, profuse sweats, memory loss, etc.

Then, from my observation, I think I am dealing with a widespread inflammation which involves many organ systems. And this information is highly suggested by clinical findings and symptoms as well as by biopsy which I've performed on many veterans in my group. To give you an example, gastrointestinal system is very involved in inflammation, respiratory system, musculo-skeletal system, skin and other systems. I wonder whether the large number of symptoms suggesting nervous system dysfunction might be caused by an inflammation. If this is the case, this inflammation could involve the nervous system at all levels. If the inflammation could be proved that it is the cause of the symptoms, one could say that we have a common denominator. It would be worth trying a treatment to eradicate the cause which perpetuated this inflammation. If this is not possible, at least to come with an anti-inflammatory medication which will suppress the inflammation and improve the quality of life.

Let me tell you several anecdotal observations which I gathered over the last three or four years. I have a person that I treat with doxycycline mostly for recurring sinus infection. In the home, the non-related sinus symptom improved–joint pain, fatigue, general well-being feelings. There is a study which is going to be kicked-off pretty soon for doxycycline for infection in mycoplasma which might possibly cause all these symptoms. My center is a participating site on this study. But those people I treated with doxycycline, the mycoplasma infection status was not known. I wonder if doxycycline, besides its anti-bacterial, viral activity, might have exerted the general non-specific anti-inflammatory effect which might be responsible for the improvement I noticed in many of their symptoms in the general well-being. I have three or four veterans who sought medical help here, in the private sector, and those people underwent what is called detoxification. And they reported that their symptoms improved, and one of my patients who went through this treatment is right here in the audience.

I think, to conclude, I would like to mention one very important thing which I've practiced for eight years now, because I've been seeing Persian Gulf veterans since November 1991. Finding and spending time and listening to the patient is extremely important and very helpful. Thank you

very much.

Dr. Benjamin Natelson, Chair

Thank you. Very good. Our next speaker is Leslie Israel.

Leslie Israel, DO, MPH
Medical Director and Assistant Clinical Professor
Department of Medicine
University of California, San Francisco
San Francisco, California

I would like to echo the concern regarding treatment, and my intent at the large group presentation was to illustrate, through cases, clinical management options, which I have been trained for and have used in practice that seem to be helpful and that is:

- Non-judgmental supportive treatment;
- Reduction of odors and irritants, and importantly, enhancing the patient's control over their environment or their situation;
- Behavioral desensitization, which can be done through bio-feedback and other rehab types which were mentioned earlier;
- Treatment of co-existing illnesses; and
- Pharmacologic treatment of symptomatic relief.

These are things which were mentioned by our Chairperson with regard to some of our goals. This is my first meeting here with the CDC and this group and I believe I'm probably the closest to completing the internal medicine residency and occupational environmental medicine fellowship so I would just like to comment on education of physicians. I think it is extremely important, but I think it can start, as was my case, during an Internal medicine residency, and I was trained at an institution where occupational medicine/environmental medicine rotation was part of the curriculum. That opened my eyes to the world of occupational and environmental medicine, and it also created my reason or actually stimulated me to choose that as my career, and I completed the fellowship. I think that one of the goals with the education of physicians is to stress the importance of that in the training in the residency program. And with that, I'll thank you.

Dr. Benjamin Natelson, Chair

Thank you very much. Mary Lamielle?

Mary Lamielle
Executive Director
National Center for Environmental Health Strategies, Inc.
Voorhees, New Jersey

I want to comment first off that most of my work has to do with civilian populations with multiple chemical sensitivity, and one of the things that I find interesting, remarkable, is with regard to – you could probably make a generalization that the majority of people who are chemically sensitive do not smoke, or have their symptoms triggered majorly by tobacco – probably find at some point that they can't at some point, drink caffeinated beverages, you know, regular Coke, coffee, that they cannot use alcohol, perhaps a diet of maybe pizza and chips is not something they can do, and they find this over a time and they find that they have to avoid those types of exposures, foods, whatever. And I'd say that the same would be true with regard to prescription medications and even over the counter medications. Many people find that they get to the point where they don't tolerate medicines at all. I think there's a serious issue, again, this is a generalization because I'm not entirely familiar with Gulf War veterans as an entire group, but it seems to me that there's a major factor of maladaptation in that area, and many might benefit from moderation and perhaps ultimately avoidance of those kinds of behaviors and might see significant, at least, changes, if not improvement, with adapting in those areas.

I want to talk also about how significant I think minimization and avoidance of exposures is, and in that framework I think it is important to be looking a patients and doing studies where you're evaluating, you're collecting data on what benefit is being derived from minimizing exposures or avoiding things, what might be the most problematic types of exposures, and again, that's a framework that I'm familiar with, primarily in a civilian population. The same thing with measuring and gaining data on the outcomes of people who make these kinds of changes and, and the critical need for educating physicians who are going to see or treat MCS patients, and I think also a team approach emphasizing, again, the importance of observing, listening, reacting. I do have a lot of concern about the education of physicians in this area, because I think a lot of times that there's a limit of what people do and don't understand about this condition, and so that concerns me a lot – what type of education will be provided by physicians, and so forth.

I want to next move to the concepts of both an environmental medical unit and also SPECT scans. I strongly think that an environmental medical unit, where you can remove people from everyday exposures, de-adapt them, re-expose to caffeine in a capsule, to low level chemicals, and so forth, is a critical piece in identifying people who are sick from low-level chemical exposures. This is an absolutely critical piece. Not only is it critical as a research tool, but I think it could be important in terms of defining treatment objectives and direction there also.

The other piece I'd say is in regard to SPECT scans. Even though perhaps the information we have is preliminary, I think SPECT scans also might provide a way to not only to research or diagnose chemical sensitivity, but also perhaps with SPECT Scans where you have perhaps an exposure or medication prior to the scan, might provide treatment regimen, treatment options. I thinks its important for Gulf War veterans who have MCS to know what their rights are in this area. That's been a lot of our focus.

The organization that I've run for about 14 years now, and that they should know or be told that, for example, HUD has policies recognizing chemical sensitivity as a physical disability, and for example, if they're in an apartment and their landlord is exterminating their apartment with organophosphate pesticides, that there are protections out there to accommodate them, and the same thing in the employment area, and education, and so forth. So I think it's really critical that they be brought into the mainstream of what has happened with regard to chemical sensitivity issues, and trying to provide protections for them that are options that might be out there.

The final thing I want to comment on is the importance of collecting more information on maybe social science areas, but basically, the consequences of being sick and so, looking at people's loss of job or maybe they're trying to continue working and maybe they're barely able to do that. So that's contributing to their level of illness, or they can't work at all and, therefore, the economic stressors involved there or lack of compensation, isolation because of the illness, family changes. I think those are all huge factors that are going to interact with how they are feeling, how they are doing, treatment regimen, so forth and so on.

I would also like to comment that in Canada, in regard to housing issues, and also clinics, but in the housing area, Canada has low-interest loans to people who are chemically sensitive to modify their house. So if, for example, a Gulf War veteran is in a house, I mean, they would have that potential of restructuring their life to some degree and perhaps minimizing their exposures. That's pretty much it.

Dr. Benjamin Natelson, Chair

Thanks so much. Bill Meggs

William Meggs, MD, PhD
Associate Professor of Emergency Medicine
Vice Chair for Clinical Affairs
Chief, Division of Toxicology
Department of Emergency Medicine
East Carolina University School of Medicine
Greenville, North Carolina

I think most of the points I would make have been touched on by other people. Throughout the decade of the '80s, the EPA's team studies have shown us that our homes, schools and offices are filled with low levels of a complex mixture of volatile organic chemicals. I think in one study, 160 different chemicals were identified and the hypothesis has been advanced that certain chronic conditions are aggravated by this constant little low-level exposure, not to mention the diesel exhaust we've got out on the highways, automobile exhaust, solvents and personal use chemicals and so forth.

Anecdotally, a lot of people, we heard Cynthia Wilson's panel discussion about how hard avoidance is, but for some people, it seems to be the only thing that works. It would be really good to get some scientific data on this issue and to have some trials on taking people out of this chemical soup and see how they do and putting them back in. In terms of pharmaceutical therapies, different things have been mentioned – doxepin, which is, what, 57 times the potency of diphenhydramine at binding the H1 receptor, whatever. It's low-dose doxine, may just be an antihistamine, but Dr. Bascom and others think that neurogenic inflammation plays a big role in these disorders and may, in fact, be correct. It would be nice to have a substance P inhibitor. I know there's some in the pipelines, but to my knowledge there are none that are available, and that's a direction people might want to go in.

And finally, like Dr. Gorin, I encourage my patients to exercise, but I'm not set up to do saunas and what do they use, or Dr. Rea, exercise bicycles and things. I'm specifically mentioning what some call the detoxification regimen that people go off and try, and in particular, the patients that I've seen that have a lot of cerebral symptoms with memory loss and cognitive dysfunction and so forth, come back and report anecdotally that this has been quite a benefit to them. It would be good to see some control trials on some of those things.

Dr. Benjamin Natelson, Chair

Thanks so much, Bill. Mike Sharpe?

Michael Sharpe, MA, MB, MRCP
Senior Lecturer in Psychological Medicine
University of Edinburgh
Royal Edinburgh Hospital
Edinburgh, Scotland

Some of the things that I would have said have already been said, and in fact, there's a rather worrying consensus. What I wanted to do is tell you a little bit about the experience of people in the UK, and I think I find myself representing that. This is Edinburgh Castle, close to where my hospital is where we're working with chronic fatigue syndrome. Why chronic fatigue syndrome? Well, as you've heard, chronic fatigue syndrome is very similar in many ways to Gulf War

syndrome. It has very similar symptoms – disabling fatigue, muscle pain, sweats, and so on. It also has a similar complexity. It's almost certainly a heterogeneous group which really poses a challenge in designing treatment trials.

One way you can go, is to take a flexible treatment, a flexible multi-component treatment, and that really was the idea of the multi-behavioral approaches, and the idea here was that this was a multi-component disorder that you have to tackle not only the person's beliefs, fears and concerns, but also mood, the way they're coping, their behavior, particularly avoidant behavior, and with the assumption that this will influence physiological processes. If we take a really simple, back of the envelop model, we say that these particular things have tied together so that if you change the way someone thinks about their illness, you'll change the way they behave, and if you change the way they behave, you'll probably alter mood and also physiology.

Now a number of components of what I would consider a good cognitive therapy have already been mentioned. One of the key ones, probably, is a general treatment ingredient before you can get started, that is, collaboration with the patient. The other problem is, and backs this issue of heterogeneity with the group is, I think you either have to take some -- so assessing the components of the illness is something that's probably important to take into account clinically and, again, is a challenge for trials.

The randomized trial that we did for cognitive behavior therapy when I was in Oxford, compared an individual 16-session cognitive behavioral treatment with standard medical care, which in the British National Health Service that means it is not a great deal. So, it wasn't exactly an active comparison group. Nonetheless, we found that in terms of a number of outcome variables, and this is showing patients' overall global ratings, but it's also reflected in patient functioning and fatigue, is a very substantial effect. But one of the interesting things that we found that surprised us, is that the effect came in late. So treatment was finished at four months, and you're seeing the maximum treatment effect was a year. The only way we can explain this is that somehow, by altering the way the patient's thinking about the problem, putting them in a more active problem-solving mode, a less avoidant mode, they gradually increase their activity, gradually re-construct their lives, and that's how the longer-term effect comes through.

I'm sorry you can't see the red very well on the side of this slide, but my colleagues, there are really three or four UK research groups involved here, this is from the Kings group in London, and they did a similar trial. In fact, I think it's fair to say it was a copy trial, except they improved it, because they had an active comparison group. An active comparison group wasn't standard medical care, which is vague and difficult to define, but was time-matched relaxation, and they found a very similar size of treatment effect, and they also found this curious delayed effect so that people were maximally improved in terms of function and fatigue at a year, when the treatment lasted about four months. So, we now have two treatment trials in chronic fatigue that have been reviewed by the Cochrane Corroboration, a systematic review, and deemed to be of

adequate quality to suggest an evidence-based treatment.

Now, the problem is with this CBT is that it is potentially intellectually a bit unsatisfying, and I think that's a problem we face with these multi-component trials. If we think of everything we've got and throw it at the patient, do they get better. Could we not be more incisive, could we not take a specific ingredient, is it really activity, is it really exercise that's the business here?

Now another of my colleagues, this is St. Bartholomew's Hospital in London, Peter White, did a randomized trial of 66 patients and randomized them either to a very carefully controlled slow-graded exercise program, or again, he had an active comparison group, just flexibility exercises, and he found fairly substantial improvement with exercise, although there wasn't a long term follow-up. And I think the important point to make about this trial is that he pre-selected the patients. These were patients who were not depressed, did not have sleep problems, so we see one of the ways of tackling heterogeneity in the patients is to choose a subgroup and focus a treatment that you think will work on that subgroup.

The moral here, if you look at another trial, this is another one of my colleagues, not a very big country, the UK, we all know each other. This is from Manchester, and being it Manchester, a bit more down to earth, you know? They just took consecutive patients and put them in an exercise trial, and of course, the problem was, they wouldn't do it. Only 23 of 67 of the patients would actually do the exercise. Now that may be because their exercise regimen was a little bit steeper, but these were unselected patients and they didn't have a big explanation, a big introduction to a collaborative approach of treatment. So, this suggests that if you take all-comers and you try a single modal therapy, you run into trouble.

Now, the other interesting thing about exercise is it appears that at least in Peter White's trial there, he doesn't improve physical fitness. It does improve physical fitness, sorry, but there's not an association between clinical improvement and improving physical fitness. So, what does that mean? It may mean that what we've got here is based in exposure program and one thing I think is the common factor between a CBT and exercise programs is, if you can engage the person, you can get them to think it's a reasonable thing to do. Exposure, actually, is the thing that makes the difference. I think the point is, though, that just putting people to exercise programs doesn't really work, it's probably not acceptable, and it's probably not a sufficient enough treatment. They need explanation, they need to have faith that this is a reasonable thing to do.

So, where I think the chronic fatigue literature would take us is, assuming this does generalize, that it is possible to make a difference, that the treatments that have worked are pretty intensive – 16, that's not group sessions, 16 individual hours of CBT works; that exercise works to some extent in carefully selected subgroups; that it doesn't work as a single modality treatment if you take all-comers.

A couple of more comments. People said, "Well, what about managing treatment now? What about the way doctors handle patients?" And of course, one of the things that emerges from this is that doctors tend to see patients in two ways. They either have a biologically identifiable disease or they're nuts, they're psychiatric patients. And as we see, back to Scotland, someone playing golf, the doctor playing golf is saying, "Tell them they only think they're ill and send them home." And even more extremely, they're seen as "problem patients" and even the psychiatrists dismiss them. That is serious. I think that takes us back to, if we're going to think about trials of improving maybe primary care physician management, if we assume that these people are going to be ill for a long time, we're hoping to find a magic cure, we also need to think of good quality, on-going management. And I think the answer there may be in evaluating ways of getting primary care doctors to assess them and manage them in a formal multi-dimensional way, rather than either just medical or psychiatric.

So that's all I wanted to say. It will be sad if we see the looking for the cause as a scientific endeavor and looking for treatment as a rather sloppy, throw everything at them endeavor. I think it is a challenge because of the heterogeneity, but I think we either take subgroups of patients and do careful randomized trials, or we take complex treatments with carefully prescribed protocols and take all-comers. Thank you.

Dr. Benjamin Natelson, Chair

Excellent. Thank you, Michael. Anne Solomon.

Anne Solomon, PhD, MA
Research Fellow, Department of Medicine
Pennsylvania State College of Medicine
Hershey, Pennsylvania

Thank you. I have one suggestion to make. I would like to elaborate on the rehabilitation model. Fortunately, in the veteran service there is a tradition of group therapy. I know that it is going to be employed, is being employed, as cognitive behavioral therapy. However, it is largely talk therapy and those of you who were at the general session know that I think we should be concentrating more in the visual area.

My own experience at the VA was to run art therapy groups for three entirely different groups of people. Some had psychiatric problems, some had alcohol-related problems, and some of them were on a geriatric rehab ward. The model is a desensitization kind of model, basically a behavioral model in the sense that, if you have a group of people for whom you lower anxiety, but then give them graded tasks that can be standardized, that move from more structured to more and more spontaneous tasks involving the visual area, that it is possible to restore function to the right frontal lobe. That is my suggestion. And along with it, the other is to have music therapy of

a very specific type, combined together with this. It's a way of cutting down on the verbiage.

Dr. Benjamin Natelson, Chair

Thank you. Kris Dahl?

Kristina Dahl, MD
Clinical Instructor
University of Medicine and Dentistry of New Jersey
East Orange, New Jersey

In the interest of time, I'm going to start before the slides come up. I'm going to be talking about work that was primarily done by Dr. Arnold Peckerman and of course, Dr. Natelson. As cardiovascular dysregulation is a possible cause of fatigue, and as war-time stress is a hypothesized cause of Gulf War syndrome, this study focused on these two factors. This study population consisted of Gulf War vets that had chronic fatigue - those who met the 1994 CDC case definition for chronic fatigue syndrome, as well as those who simply had idiopathic chronic fatigue that didn't meet those criteria. There are also controls.

We studied 51 patients and 35 controls. They were similar in all these listed factors except for education and smoking, which were controlled for. One way of looking at war-time stress is by looking at the incidence of PTSD. The Gulf War vets who had chronic fatigue had 31% incidence of PTSD, whereas the controls had only a 2% incidence.

We examined cardiovascular responses to cognitive stress including the mental arithmetic test and an evaluative speech task. Three groups were compared. Gulf War vets that had chronic fatigue syndrome and did not have PTSD, those who had chronic fatigue and did have PTSD, and controls. Both chronic fatigue groups were found to have smaller increases in blood pressure in response to cognitive stressors than did the healthy group. The Gulf vets that had PTSD as well as chronic fatigue, had smaller increases in blood pressure during speech than did the chronic fatigue group that did not have PTSD.

This slide shows the change in systolic blood pressure, which is seen after the cognitive stress that we just talked about. We see on the right the decreased response of systolic blood pressure in the Gulf Vets with CFS, the ones that had PTSD in addition, are on the far right and you can see that's clearly decreased. In the cold presser task, there were no significant differences in the groups. This tells us that the peripheral vascular system is probably working alright, suggesting that the abnormal response may be due to dysfunction of the central nervous system. Within the patient group, hyporeactivity to cognitive stressors was highly predictive of poor clinical status on the day of testing, as assessed by a particular checklist called the De-activation Checklist. The autonomic testing included orthostatic challenge and assessment of the baroreceptor reflex.

On standing, the patients that had CF and PTSD had a steeper fall in systolic blood pressure and failed to show a systolic blood pressure overshoot on standing. Those who had merely chronic fatigue, and did not have PTSD, were no different from controls. In contrast, in tests of baroreflex function, it was the Gulf vets without PTSD, who had an abnormal response, showing a decrease baroreflex sensitivity.

In summary, Gulf War vets with chronic fatigue may have inadequate cardiovascular responses to stressful behavioral activities, which could have metabolic consequences consistent with fatigue. Cardiovascular dysregulation seen in those with chronic fatigue is worsened by the patients also having PTSD. These effects are surprising in regard to PTSD because previous research has suggested an autonomic over-reactivity. The fact that cardiovascular hypo-reactivity was correlated with poor clinical status on the day of testing suggests that treating cardiovascular hypo-reactivity may result in clinical improvement. The orthostatic hypotension seen in the patients with Chronic Fatigue and PTSD suggest that treatment along the lines of vasoconstrictors and agents that increase blood volume may be beneficial. These treatments are oriented to a particular system of the body rather than being non-specific therapies, and you would term these "evidence-based" as mentioned by our Chairperson.

Dr. Benjamin Natelson, Chair

Thank you very much. We're now at 5:28 on my watch. Before I open, and I'm not sure if we're really going to have time to open to questions, because the whole next session will come from the audience. So, let me just be sure that the workshop is willing to be on the same page as me, and if not, suggest an alternative page. I have suggested that, in order to force us to try to come up with trial recommendations that are short- and long-term, that we divide ourselves into four groups. Let me just quickly ask for alternative organization ideas. We have a major task upon us, to come up with actual lines of recommendations, I think that we have to operationalize our thinking so that we can move ahead.

Dr. Michael Sharpe

Mr. Chairman, just thinking of the, sort of, the NHS R & D in the UK puts out calls for things and I think it's important that we specify, as they do, the criteria for adequate design and so on, instead of just giving them a long list of agents that we think might do the job.

Dr. Benjamin Natelson, Chair

Absolutely. That was one of my goals, Michael. We can't just come up with bright ideas. They have to be evidence-based and there have to be appropriate design issues. If we can't do a good design, then even if it's a tremendous idea, we can't recommend it. So, I hear you. Well then, I will ask the committee. I'll ask you Mitch, if we just go around, let me remind you that I came up

with a list of four possibilities and that was:

- Drug or Pharmaceutical Possibilities
- Rehab
- Mind/Brain/Psychological
- Other

Dr. Rebecca Bascom

Well, that "Other" was really "Avoidance" Ben. Avoidance of foods and . . .

Dr. Benjamin Natelson, Chair

Well, that was an example I gave. One other example that I heard twice that would fit into the "Other" was this bringing people into this chamber idea. But that's fine. That would fall into that group. There might be, again, we haven't heard from our audience. They might have other ideas besides avoidance. Stu.

Dr. Stuart Brooks

I don't know whether this fits into, but we have basically four methods or approaches and we're going to look at outcomes. And when you look at outcomes, there are a lot of things that determine outcomes. That is, you're providing a certain treatment. If you look at the model of structure, process and outcome, there's a lot of things, for example, structure, where the test is done and the persons giving it, and the process – how they're trained, whether they believe in it, family's input. And then we look at the outcome. There are so many things that affect the outcome, so another thing that I was going to -- is to look at, sort of, organization.

One of the things that I was going to mention, is that I didn't realize until this morning when we heard about some of the veterans, the tremendous anger that there was at the veterans' group toward the Department of Defense. And it reminds me, doing occupational medicine, seeing a lot of occupational problems over the years, particularly sick buildings and back injuries, and where there is, 100% of the time, and it influences the outcome, is the psychosocial – the issue dealing with the relationship between the patient and some entity they think has not done their job, that they have really misrepresented their country. And unless you deal with that issue you're not going to solve it. And so, the issue of how the VA deals with these veterans, and they're going to have to bite the bullet, as I tell employers, and do things that are not normally done, probably a critical feature is how the veterans' organizations handle the veterans, the type of treatment they give and the responsiveness they provide, is going to influence the outcomes.

Dr. Benjamin Natelson, Chair

Well, that's critical to take into account. The short-term therapeutic trials that we do certainly need to look at veteran satisfaction. And certainly you're right – the veterans we heard from today are certainly not satisfied. Let me just ask if we can -- yes?

Mrs. Mary Lamielle

I have some concerns that some of the issues I mentioned, the avoidance strategies, environmental, food sensitivities and all these things are in a category called "Other."

Dr. Benjamin Natelson, Chair

Do you want me to change "Other?"

Mrs. Mary Lamielle

Well, I do want you to change "Other", and I'm not sure what we're going to say, and I think "Other" should be another category, but I have a sense that if we move...

Dr. Benjamin Natelson, Chair

The only reason, organizationally, I'd like not to do that, is I'd like to leave that there. If we hear tomorrow that there are so many other things that we have to have another category, let's do it.

Mrs. Mary Lamielle

Let's at least name it tomorrow. There's a sense that when you call something "Other," I think, automatically minimizes it, if not diminishes it.

Dr. Benjamin Natelson, Chair

Well then, let's name it. Let's call it "Avoidance" ...

Dr. Stuart Brooks

I heard the term "Multi-Modal Approach" mentioned several times, would that fit under "Other?"

Dr. Benjamin Natelson, Chair

Actually, no, that's a problem. Well see, now we're getting bogged down in details. Humor me until tomorrow, I hear you, well, we will do it. OK, so let's go around the room. The problem is, this has got to be every one. I mean, we hear the veteran. We doctors -- that's part of this

education issue that I would like to be one of the goals. How do we educate the doctor to care about what his patient thinks?

Dr. Stuart Brooks

It is not only the attitude of the VA, the education of physicians and the whole organizational sense that's involved in carrying out these different treatment trials. Because there are so many other influencing things, and looking at those other influencing factors is maybe a category of it's own in evaluating the outcomes.

LTC Charles Engel

One thing I heard in listening to you talk, and it may have come out of my head and not out of your mouth, is just the idea of the structure of services provided, that there are ways in which – of interest to me is how some of the measures that we are talking about here might be provided in the context of primary care and I would call that "Structure of Services" which gets at how the VA, or how DoD, or whatever healthcare organization might be out there providing care, would address these things. And that would be a category of interest to me.

Dr. Benjamin Natelson, Chair

Although I must say again, these issues have to be parceled into every one of these treatments. These are the psychosocial issues of the doctor/patient relationship, and are critical, and they have to be one of our goals. What I have done, artificially, is tried to break it up into manageable groups. But our goals, I will remind you of, are short-term. What can we do now? In the next year or two? And try to keep it evidence-based, and try to do it in a way so it is not anecdotal. That's number one. And then number two, long-term, where we come up with random trials, and then last, a way to educate our junior physicians so they are aware of these things and are not rejecting or denigrating. I would like those to be our mission. I need to go around and get a vote and see whether ten people want to be in one and we just need to get a sense.

Dr. Rebecca Bascom

I would strongly support Stu's addition, because I think in the field of toxicology and occupational medicine, the interrelation of the individual to the organization is a discipline that can strongly influence outcome.

Dr. Benjamin Natelson, Chair

So, I'm then a minority? This is not involved in -- we don't have to worry about number five in every one of these? It has to stand alone?

Dr. Rebecca Bascom

One of them, the item for the drug, the question is should the doc prescribe drug A?

Dr. Benjamin Natelson, Chair

Pardon?

Dr. Rebecca Bascom

The question you're trying to answer in Category 1 is, should a doctor, should a clinician prescribe drug A? And under what circumstances is it effective? And in item number 5, the question is should there be a rehab program that is available to any person who wants to be part of it? Should there be an ombudsman? Should the way that the VA structures how people get into the system be different? Much more macro.

Dr. Benjamin Natelson, Chair

Okay.

Dr. Stuart Brooks

If you look at the drug treatment, the drug treatment in itself is not the only thing that influences whether a person gets better. How that person responds to their physician, how they feel about the interactions with their family, children. This whole process is -- there are many, many things that influence outcome. Unless you identify them, what I mean is, I did not realize until Mrs. Brown got up in tremendous anger that, and all the other voicing of anger, that's a major problem, and I see that in many of the occupational problems and until you deal with that, you're never going to solve the problem.

Dr. William Baumzweiger

I'd like to reinforce that. What the veterans are furious about, absolutely livid, is first the categorical, total denial that this existed, and then blaming them, saying it was all psychiatric, or they were malingerers, or they were goldbrickers, or then breaking it down into stupid symptomatic categories like, "You've got stomach problems, or a lung problem." I mean this is idiotic medicine. And then finally, Dr. Rea just left the room in a rage because he's been helping people. He just up and left and he and I have been talking, maybe you saw us, he is really upset, because the issue should be, well, one of them, these veterans know that there have been doctors out there who have been helping people, who had the financial resources to get to them. Myself, Dr. Baumzweiger, out in California, Dr. Rea, Dr. Hyman, there has been help. And the DoD and

the VA, for the last four or five years have been systematically firing doctors who propose these kinds of treatments, getting rid of them like they got rid of me, a number of people, Shayevitz, and other people. They're furious, they're enraged, they're dying, they're in wheelchairs. You're going to walk home. Most of these people are in wheelchairs and they're gonna live no more than five years.

Dr. Benjamin Natelson, Chair

Doctor, I think that what we have to do then, is try to grapple with these realities in some kind of concrete way. We have been urged to come up with concrete, brief and single line recommendations. So, alright then, I guess the issue is then, micro versus macro. Just from what you said, macro has to be in micro. So first of all, if 13 of us split into five, that's two and a fifth, so we need few rather than more, so Chuck, help me out. This goes out. OK, unless there's another therapy, unless there's a new therapy that can fit. [Simultaneous discussion].

LTC Charles Engel

What bothers me is, what is this? I am not real sure.

Dr. Benjamin Natelson, Chair

Well, is CBT the only way that we can address. . .

LTC Charles Engel

I see CBT as here.

Dr. Dan Clauw

Combine these two.

Dr. Michael Sharpe

Should we combine them rather than delete them.

Mrs. Mary Lamielle

Can you re-read the list.

Dr. Benjamin Natelson, Chair

So we have drugs, which is physical medicines, which can be homeopathics, what ever.

Mrs. Mary Lamielle

We have drug now, not pharmaceutical, but just drug, is that what the category is now?

Dr. Benjamin Natelson, Chair

Pharmaceutical, well I don't know the difference actually, medicine that you take in your mouth or that you inject. [Simultaneous discussion]. Ok so this is pharmacologic, alright, so let's do it that way. Do we want to have instead of rehab, non-pharmacologic? [Agreement], Ok, non-pharmacologic. Thank you Nancy.

Dr. Rebecca Bascom

Excuse Me. Which category will contain forms of treatment commonly thought of as alternative?

Dr. Benjamin Natelson, Chair

Probably non-pharmacologic, I would think. [Simultaneous discussion]. Well, vitamins and minerals are things you ingest. So those would be pharmacologic. [Simultaneous discussion]. I am going to say, obviously homeopathic is not pharmacologic, but instead of getting into arguments about this, I don't know, does someone have another word?

Dr. Rebecca Bascom

How about pharmacologic and homeopathic in category one.

Dr. Stuart Brooks

What about alternative.

Dr. Benjamin Natelson, Chair

No alternative is not, what I am trying to do is something that is put into the body, either through the mouth or injection, or what ever. That is what I am trying to get at. Something which is drug, chemical, something like that [Simultaneous discussion]. We are going to try to make this happen, this is hard.

Dr. Stuart Brooks

Vitamins are part of a whole program, and it probably goes more into the non-pharmacologic.

Dr. Benjamin Natelson, Chair

I think if you ingest or you inject intravenous vitamins, you ought to be able to do a trial to see if it works, otherwise it is anecdotal. Lets push on. We have these two. We have "Other" which is a problem, we know already. I am prepared to change "Other" now. [Simultaneous Discussion]. Alright we will call this "Avoidance/Elimination." Number four will be will be if individuals are unhappy with any of the others again, I don't know how we go into "Other" because at least, until now, we haven't come up with any other. So, here we go around the room, and number five is "Macro," again that big sort of, what is influencing the health and the interaction of the patient? Dr. Gordan, what would you choose?

Dr. Victor Gordan

Before I choose, I'd like to make a short comment. Macro. You can't realize how many VA hospitals don't have a well-structured primary care team for Persian Gulf. That should be addressed very specifically. Pharmacological.

Dr. Benjamin Natelson, Chair

Mitch, I need you to be the score keeper so it's not 12, 1, 0, 0, 0, then we are in trouble. [Simultaneous discussion while panel members decide which topic they would like to focus on].

Dr. William Baumzweiger

I would like to just point out that this is happening because of wide leadership and interaction with the audience. If this had happened 6, 7 years ago, we would not be sitting here today. We would have solved the problem.

Dr. Benjamin Natelson, Chair

Let's not pat ourselves on the back. We have not gotten far. We have now run out of time. What will happen tomorrow in our first session, is that it's up to you and the audience. You will hopefully have signed up so we could figure out the 8 minutes business for you. Do we know how many people want to speak tomorrow? There are at least 20 people signed up so that means, wait, let me tell you what that means. That's a problem. Since here we had 13 people for 8 minutes, that means you should organize your thoughts to take, I apologize for this, but I am not the organizer, I am the person who is just trying to make this happen, and I am sweating to please try to confine your talk to five minutes and if we can give you more, we will. But I don't see it in the cards. If there is more than 20 people signing up, I will have to reduce this, but

please understand that this is not me, I am just trying to make it happen. Thank you.

The session was adjourned.

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Day 2 – Monday, March 1, 1999 - Morning Session

Dr. Benjamin Natelson, Chair

Everyone in the audience who has his or her four minutes, if that individual can tell me his short- and long-term goal, I will write that down and you will have an impact. If you just speak broadly without any specifics. I'm going to turn it over to Mitch. There are very few people here, but you can tell them about the rules of the presentation.

Mitchell Wolfe, MD, MPH
Epidemic Intelligence Services (EIS) Officer
Surveillance and Programs Branch
Division of Environmental Hazards and Health Effects
Centers for Disease Control and Prevention
Atlanta, Georgia

I just want to go over the ground rules so everyone knows where we're going. These were passed out in your conference papers:

- Please state and spell your name and organization whenever you speak for the record, because there's going to be a transcript;
- Every individual has the right to be heard and you've got to sign up;
- All opinions are valued and respected;
- Only one person speaks at a time;
- Talking in the audience while others are speaking is discouraged;
- Direct responses to the subject matter and not to the individual;
- Keep voices in a neutral tone;
- Support and empower each other to achieve the needed results;
- Repetition of previously stated points is discouraged;
- Use of acronyms is discouraged;
- The purpose of the conference is to develop research recommendations, therefore, comments should focus on the research issues;
- There will be a time limit for each speaker of four minutes.

Dr. Benjamin Natelson, Chair

What I'll be doing is asking each speaker to try and tell me his or her long- and short-term goal. Right now we have five groups: Pharmacological, including anything that would be ingested or injected; Non-Pharmacological, and there is a move from the panel to move that from Macro, and we obviously can work on that later; Avoidance; and Other.

James Way, PhD
Professor
Texas A & M University
College Station, Texas

There's one chemical here, pure chemical, it's well-defined and may have been causative, and yet very little has been done on this which is sort of appalling. This is the use of sarin. There are enzymes that can hydrolyze sarin, and very active enzymes. This has been done against the pyridostigmine, it can be done against sarin. By using the enzyme and encapsulating them so that they stay in the body a long time, such as using the liposomes and the use of other carrier systems, it's possible to get rid of the sarin.

In this way, you have your short- and your long-term factors. As far as the short-term research, if you have a toxin, you should try to get rid of it. And the second thing that you should do . . .

Dr. Benjamin Natelson, Chair

Can you be concrete so I could write something down here?

Dr. James Way

Sarin. Long-term, carriers, lipo. The short term goal is get rid of sarin from the body. Destroy the toxin. For the treatment, for those that are poisoned with sarin . . .

Dr. Rebecca Bascom

Can you suggest how to go about doing that?

Dr. James Way

I just said, I'll repeat it. You have an enzyme, a recombinant enzyme that can hydrolyze the sarin very rapidly.

Dr. Rebecca Bascom

So, you would administer that enzyme? Is that the treatment trial?

Dr. James Way

Yes, and use a carrier system so the enzyme will stay in the body for days, weeks or months, and if you get rid of sarin, you would get rid of your problem.

Dr. Rebecca Bascom

Do you know what enzyme?

Dr. James Way

The enzyme is OPA. Hydrolase is the one for pyroxene. It's OPA and Hydrolase which is for sarin. And this is a long-term therapy and short-term therapy. You need the long-term because sarin distributes in the fat tissues and it takes a long time to come out.

Dr. Benjamin Natelson, Chair

Thanks very much.

Wendy Wendler, MBA
National Board, Special Projects
Desert Storm Justice Foundation
Dallas, Texas

I was a Red Cross worker during the Vietnam Era. I was exposed to the defoliantes they secretly used in the Republic of South Korea on the DNZ area, so I've been doing this a while. I'm encouraged by the notion that we're talking about treatments that are hopefully real world oriented and result-oriented. I have an MBA in health management and I'm always struck when I hear, as in the Veterans' Forum last night, that we have professionals in our midst as patients who function on both sides of the bed in the healthcare community. I'd really like to see, for want of a better word, a parallel, in that we are looking down the road far enough in the long term to know what we want to do in the short term, but start them simultaneously or in a coordinated manner.

I'd like to use an example of Dr. Hyman's study on the strep strain that he's known about for thirty years and one of his points, I understand his proposal, I'm going to use that as an example, was to take the $3 million for the 3 dozen vets, but he also made the point to me, "I could screen everybody for $3 million." And maybe I'll just make some generalities here. Whether you're going to do the sauna de-tox attempt at Health Med, whether you're going to take some of the nutritional supplements that I've taken and kept myself going with for ten or fifteen years, let's do it in the short-term to see some immediate results. Let's say that we're going to have at least a preliminary study at least in so many months, and make it months, maybe not weeks, but certainly not years. And the consumer review group, whatever you want to call the Desert Storm advocates that are involved in every study, as they should be, say, in three months, we get a preliminary report, you don't get any more money. I understand they do give the money out in stages. It's sort of like a painter's contract. If they don't paint the garage they don't get the money for the rest of the place. To say that there's a preliminary report, there's certain

intermediary reports.

The frustration, I think, for some of us in the audience, for instance, this morning, is to hear Claudia Miller say something that somebody else should have been listening to who was getting coffee. There seems to be one of the oversights in coordination that we searched for in the Persian Gulf Coordinating Board, for example. So, I was particularly interested yesterday in trying to find a category to put nutrition supplements in. I brought some MRE's for everybody to taste from my Army/Navy store. We're very concerned that according to General Schwarzkopf's book, which I've excerpted, when you take all of the environmental and health mentions in Schwarzkopf's book about the Gulf War, you see he was very worried about the food and the footwear the first week he got to Saudi. So I think all the clues are here.

I'm also a theater arts major. My tendency as a director of a play is to say, "I hear all the actors and they're not rehearsing together." So, my general statement is to take the short-term and know what the long-term -- I don't say we have to skew the study where we think it's going, but we have to be able, in certain stages, to know that when we get done. Somebody's going to have learned something and take what we've learned as soon as possible and begin finding ways to factor it into what everybody else is doing.

Dr. Benjamin Natelson, Chair

Very good. What I'm looking for, as much as possible, are concrete plans, that's helpful.

Paul Gruendler, BAEd
Member, RSES
Rising Fawn, Georgia

Do you need some public input? I'm from Rising Fawn, which is right up on the Tennessee/ Alabama/Georgia line there. My background is I'm a Vietnam veteran, I was in the military police, and the 23rd Infantry, and the 101st Airborne right at the winding down of the war, and was there in1971, came back, and was basically self-afflicted by numerous toxics. But I got over those, thank the good Lord. Then I found myself, almost twenty years later to the day, getting off an airplane in Ad Damman with elements of the 196th Field Artillery Brigade. That was Desert Storm. So, Southeast Asia to Southwest Asia, twenty years apart, and since that time I have felt the symptoms of fibromyalgia, along with the VA's assessment.

I went to the VA at the invitation of Bernard Rostker, and took the test and went through the evaluations, and got the diagnosis of fibromyalgia, and then got a little bill in the mail, but I wasn't really consulted about my symptoms or anything else. I was there on a Saturday morning, and the clinic closed here in Decatur. I didn't get anything back on my blood work or anything else, just a little cursory note that said, "You're fine." Well, I didn't really believe that because I

still feel certain things are wrong with me, so I was able to, thanks to the good folks of my father's estate, to go to the Mayo Clinic in Scottsdale, Arizona where I was looked at by some of the MDs out there. One of them, and I can't recall his name right now, has seen a number of cases of self-referred Gulf War syndrome, and he, in his report, which I have a copy of, said that my symptoms were not as severe as other Gulf War veterans that he has seen. And to that, I may publicly state, and for the matter of public input, that I would attribute it to my wife, who has been the proprietor of a health food store since 1989. She has been pumping me with every vitamin, mineral, protein supplement you can imagine, so all I can give you is anecdotal information, really, but I can say, I believe that my symptoms are being managed so that I can function until about 2:00 in the afternoon everyday. I'm in broadcasting now, at WKWN, AM 1420 Radio Georgia, and I work until about 2:00 in the afternoon, then I go home and fall asleep. Then I get up and do a little refrigeration work. [A request came from the audience for Paul Gruendler to provide a list of what he is taking, which he agreed to do, later on.]

Robert T. Wolfertz, MA
LT. COL. Marine Corps (Retired)
Desert Storm Justice Foundation
Bedford, New Hampshire

I'm a Lieutenant Colonel, United States Marines Corps, retired. I'm not a doctor, I'm not a researcher, and quite frankly, I feel a little bit out of my element here this morning because I'm not sure that your expectations and my input are going to meet, but hopefully I can go where you want me to go here. In fact, yesterday I was able to figure out what an N of 1 is, I know what an etiology is, and I think I know what a modality is, so maybe I'll be able to provide some meaningful input here.

For those of you who were at the Veterans' Forum last night, thank you again. For those of you who weren't, just a brief background. I served as the Executive Officer for the 4th Marine Regiment. We attacked in Kuwait just two days before the official start of the ground offensive to clear the way for the 1st Marine Division's mechanized armor assault. In the process of preparing for that attack, and during the conduct of that attack, I was exposed to a wide number of, what I subsequently learned, were contaminants and toxins that could have a detrimental effect. I began experiencing symptoms post-hostility like lower-back pain, a rash on my foot, which came and went over the next several months. I managed to be well enough to retire from the Marine Corps and then started to become more symptomatic over the course of the next six months. Joint pain, fatigue, short-term memory loss, the rashes, any number of things. I happened to be fortunate enough to appear before the Presidential Advisory Committee on Gulf War illness, and in the process of doing that, met a woman who knew of a detoxification program in California and recommended I get a hold of that clinic. They were offering it on a trial basis to afflicted Gulf War veterans. So, I called the clinic, spoke with the Director, went through their detoxification program . . .

Dr. Benjamin Natelson, Chair

Can you tell us in about one minute what the detox is, so I can write it down?

Mr. Robert Wolfertz

Yes, it's a program of exercise to get things flowing, and increased doses in a sauna to get the bad stuff out of your system while replacing it with vitamins and mineral supplements and oils. So things were removed from my fat tissues and replaced with good stuff. Over the course of seventeen days, I noticed a constant improvement, until the point of the seventeenth day, where I felt wonderful. That was 2 ½ years ago, and I continue to feel wonderful.

Dr. Benjamin Natelson, Chair

Super. To sum up then, it is exercise and heat, to act sort of as a purgative, if you will, to get the bad stuff out, as you put it, and then supplements. And you're continuing with the supplements?

Mr. Robert Wolfertz

That's correct.

Dr. Benjamin Natelson, Chair

Was it intravenous vitamins or by mouth?

Mr. Robert Wolfertz

By mouth.

David Root, MD, MPH
Medical Director
Occupational Medicine Group
Sacramento, California

I am the Medical Director for the Health Med Detoxification Center in Sacramento, California where Robert Wolfertz went through the treatment program. I am proposing, and I don't know which of your five groups we would fit into, maybe "Other," but I'm proposing a study to start with at least 100 to 200, appropriately, exposed Gulf War veterans, that is to say, those who have known chemical exposures, which is probably going to be most of them, to go through a detoxification program.

Dr. Benjamin Natelson, Chair

Can you be more specific? What is the detoxification program?

Dr. David Root

Okay, let me go through it for you. Basically, the rationale behind the detoxification program is to mobilize those toxicants which are stored in the fat, and therefore are being released periodically under certain stressors and causing problems, similar to what Dr. Miller was talking about this morning. The way we do this, is we use niacin as a mobilizer of fat, it also causes a peripheral vasodilatation, a flushing effect, which we use, which I'll describe in a moment. That's graduated from 100mg up to as much as 5,000mg, depending on tolerance, but we start off at 50 or 100. We use aerobic exercise. They take the niacin, then they exercise to tolerance for 15, 20, 30 minutes, whatever they can tolerate, getting the blood flowing, and at that point, we put them in the sauna. They're in and out of the sauna over a four to five hour period, and during this time, they'll stay in the sauna and they're sweating very profusely because of the effects of the exercise, the heat, and the niacin. During this period of time, when they're fatigued or heat stressed, they'll come out of the sauna, cool down, replenish fluids and electrolytes. We also give them, as Colonel Wolfertz mentioned, an all-blend liquid oil which they take by mouth, to tie up any of the toxicants which are secreted into the gastrointestinal tract to keep them from being re-absorbed by the bile acids.

Dr. Benjamin Natelson, Chair

What's the oil, Sir?

Dr. David Root

It's an all-blend liquid oil, it's cold pressed liquid oil which you can buy off the shelf, and over a period of days, they stay on the program from anywhere from a minimum of usually about 2-3 weeks up to, well, the longest Gulf War vets we treated went for 73 days, no breaks, seven days, right on through. Over a period of time, what happens is that about 15% of the toxicants come out through the skin, with the sebaceous sweat, and we think about 85% come out through the GI tract, tied up with the all-blend oil. Obviously, some of it is going to come out through the kidneys, but we haven't had a chance to look at that. This is peer-reviewed, I have a copy of a short description of the program, which I'll give to you. But I'm proposing that we come up with funding somehow or other, to put in the neighborhood of 100 to 200 Gulf War vets through this kind of a program. I put three through. That's not a lot, but the similarities are so great to the other chemically-exposed people that I've been treating for 17 years in Sacramento, who had excellent results and one of your panelists has been, at least partly, through the program. This is a peer-reviewed type of a program and I think it deserves much more in-depth look-see with

oversight from a panel of experts as yourselves, and document exactly what this can do for these people. We've helped chemically-sensitive people and others folks who've had other types of chemical exposure.

Dr. William Baumzweiger

You know, I'm a neurologist and psychiatrist and I told the VA about four years ago this was a neurological and immune problem and they rewarded me by dismissing me from my fellowship in neuromuscular disease. I subsequently have done evaluations of these people and found that they have had very extreme levels of not only psychiatric symptoms that don't really fall into any clear psychiatric syndrome, but they have a lot of neurological problems as well as inflammatory processes spreading throughout the cell-mediated parts of their bodies. Excitability, inflammation, demyelination of practically every part of the nervous system characterize this disease and I don't have the time to go into that here, but I concluded that the neurons were becoming inflamed because there was damage to the NMDA and probably other calcium channels, because they're the most complex and most easily damaged by immune and infectious attacks. The infectious being viruses and funguses that these people got because they were exposed to toxins, and probably experimental vaccines that were very bad for their immune systems.

At any rate, they were immune-suppressed, their brains were inflamed, their immune system attacked the brain probably in the brainstem area and that's what common with chronic fatigue syndrome and Gulf War syndrome and fibromyalgia and multiple chemical sensitivity. They all have to do with the brainstem and different variations of immune attack and neurological defense or neuro-psychiatric defense. I did a calcium channel-blocker study, showing that the orthostatic tachycardia they have, which is usually about an increase of 20 beats per minute when they go from sitting to standing, Gulf War veterans, 22 actually, can be cut in half by using Plendil, which is felodipine or Nimotop which is nimodipine, anywhere from 30-60-90mg per day for the Nimodipine, I 'd say Nimotop, 30mg, 3 times per day. This was published, along with a factor analysis of 27 other associated symptoms and interestingly enough, 17 of the 27 symptoms improved to some extent in five separate clusters along with the improvement in the heart rate stability. I have since then added Gabitril, 4mg, three times per day, because it's a GABA agonist which reduces inflammation in the neuro circuits of the brain and spinal chord and perhaps, peripherally. On lab testing, and I recommend certainly lymphocyte testing and testing for viruses and funguses, especially the IgGs because these people do not make IgMs. And you can forget what the infectious disease guys say. IgGs are really important. It's just been shown that IgG for Herpes 6 is associated with multiple sclerosis plaques. Multiple sclerosis is probably reinfection with IgG or at least as part of its mechanism.

So, I recommend calcium channel blockers, Gabitril, full labs with lymphocyte profiles, fungal and viral panels and antibodies to look for myelin smooth and striated muscle antibodies, stomach and

thyroid antibodies.

Dr. Benjamin Natelson, Chair

If you can get that peer-reviewed paper, it will be helpful. Thank you very much.

Venus-Valery Hammack
Womens' Liaison
North Shore Veterans Counseling Services
Lynn, Massachusetts

U.S. Army, 24 years, now medically retired. Under the subject of treatment at this conference, I wanted to make the input that not having the scientific expertise, I'm not going to pretend to tell you which protocol to do, but one thing that I can do as an entry- level medical trainee, technician, technologist, hemodialysis technician, is that at this point in time, what would benefit the veterans, is to see that this study money is used on actual veteran trials, not the mice, not paper statistics. We want to see, at this point, because there's so much good input, we can't say that there's not proposals out there and to just continue the study process, seeking new proposals, new methodologies. I think that's wasteful at this point. We veterans would like to see the trials occur. Whether they fail, we have learned something. But, at that point, people have the hope to go forward, and the trials that we think at the last minute would not turn the rock or turn people's corners, might be the one to occur. So, I'm asking for veteran participation in any trials that are being funded by the monies that were allocated for '98/'99 services. Thank you.

Joseph Miller
North Carolina National Guard
West Jefferson, North Carolina

I was assigned to the 1450th Transportation Company, 19th Airborne Corps. I have already, on my own, taken the mycoplasma therapy that I think is going into clinical trials almost immediately. It's helped me a lot because I'm working, I'm getting better. It's not all of the solution, but it's part of the solution. I've listened very closely to the multiple chemical sensitivity things that we've talked about this morning and over the last two days, and I've related those things to how my health has been over the last 10 years, 9 years, whatever it is, and based on what I know about my health history, and the things they talked about, and the working mechanisms behind these things, these things sound very promising to me. I haven't gone into it in detail to be able to recommend what works best, but the chemical sensitivity, in my mind, is also part of the problem because you're dealing with a much larger exposure, possibly biological, possibly chemical, possibly contagious. There's a lot of different things. But a lot of the things that I've heard, as far as the speakers in the main thing up there, they make a lot of sense to me based on what I know about my health over the last 10 year. Whatever you can help them with, do it.

Joseph P. Poe
President/Founder
United Veterans of America
Dunn, North Carolina

Good to see all of you brilliant people again. On the treatment side, I heard someone say we have overlapped some. We requested, a while ago, almost a year ago, straight to DoD, you all are CDC now, different picture, except for you, Sir, Dr. Engel. We did request a mandatory baseline. That's what all of you doctors, you researchers need, what you say for every study – baseline, baseline, baseline. We requested a strong situation which would have crossed over the boundaries of political sensitivities for both the DoD and the VA. It was really quite a very simple thing. The veterans who have already been through the VA system which, DoD had cleansed their hands of them at that time, who had fell under the undiagnosed category, such as myself. My doctor is here today. Dr. Laker, where are you? Please rise. Let them see you. She's doing as much as she can with what she can do at the VA, with the funds. Alright, now, we crossed the political boundaries. You all deal with it all the time. I watched much politics here in a couple of days. Take those who are undiagnosed of etiologies. Do mandatory SPECT scans, do mandatory MRI, do mandatory DU testings. OK? There's nothing to lose.

Dr. Benjamin Natelson, Chair

Mr. Poe, can you repeat the last thing?

Mr. Joseph Poe

I will try my best. Okay, again. What I say, I know this is not treating but it is cutting through the stuff to get to treating. We did ask, we requested of DoD, Dr. Kilpatrick and Joe Gordan at the time, in a five hour meeting in Washington, D.C., and then we brought it up again in North Carolina. At the time, it was approximately 1,500, I think it's around 1,700 or 2,000 now, that are with undiagnosed. Now, that is anywhere from 0% rating to 100% rating, and even with some of those ratings, are not being compensated to feed families or take care of themselves, but that's another thing. We're dealing with treatment here, I'll try to stay on that. Somebody kick me if I do not. The mandatory baseline that you need, that I can see -- I'm not a doctor or a researcher, I'm just a dumb old Sergeant, is do the SPECT scan. Whenever the neurological symptomology is presented, cut through the garbage. If the MRI shows nothing, and a CAT scan shows nothing . . .

Dr. Benjamin Natelson, Chair

Thank you very much, Mr. Poe.

Mr. Joseph Poe

Did I go too much?

Dr. Benjamin Natelson, Chair

No, you're just there. We'll go to the next person on the list. Dr. Petty.

Frederick Petty, MD, PHD
Professor
University of Texas Southwest Medical Center
Dallas, Texas

I'm Fred Petty from Dallas, Texas. My colleague, Martin Cram, was not able to be here, which is unfortunate, because he's a graduate of Charles University in the Czech Republic. This is just a little poem I wrote to celebrate this meeting, but you can get that off our web site. The statement of the problem, we don't need to spend any time on that, nor do we need to worry about who to blame. The Gulf War syndrome is a brain disease, ergo, a mental illness and its etiology is chemical, which is saying nothing. Many brain chemicals are involved. The data suggest that its not 100 or 1,000 syndromes, but probably five or six, maybe three. This is just a hypothetical profile. I propose in the short-term, about six or seven months of intelligent animal model testing, and the models are available. If you don't understand that a rat is a lot more like you than you'd like to admit in public -- these are just some of our future plans. In terms of where to go, this is easy. Start with Depakote, tricyclics make these people worse. Treat inflammation, treat infection, and then worry about neurotransmitters. We actually submitted a proposal to you know who, which was ignored for nine months, so they could give the money to somebody else, and in this age of algorithms, I even have an algorithm, which is Algorithm B for symptomatic treatment. We believe in a structured clinical interview, and basically, we have a series of chemicals that we would propose to try. After Depakote, I would recommend amphetamines, or Wellbutrin, which is an amphetamine-like compound, perhaps in combination with Depakote, and antibiotics, which are cheap, and work, and you can take them. I take an antibiotic every February whether I need it or not. I would welcome comments. I've got the world's easiest address on aol.com. Thanks.

CDR David W. Seipel, MA
Naval War College
Newport, Rhode Island

I spoke last night, and I think I said what I pretty much wanted to say, but one thing I would want to stress, is that with the testing that's being done in the major centers and D.C., and even with the VA, there's a lot of people that are in the outlying areas that are not being involved in the testing. I went through CCEP Phase I and II in D.C., when Dr. Clauw needed patients who had

FMS who could fall into a study. No one ever sent me a letter stating that he had a test going on that might be of benefit to me. So, I went out and found it through the web page, and my wife, going to some of the conferences and talking to people -- so the information is not getting out. I mean, I can't believe I'm one of the few people that's a Gulf War veteran that has fibromyalgia. There should be people beating down Dr. Clauw's door to be looked at, and it's not happening. So, I don't know where the problem is, either DoD or VA. I have a lot of friends, active duty, that are sick, so I don't see how one can say that there's no one on active duty that has any of these problems. For the rest of my time, I'd like to defer to the Denise Nichols. Thank you.

Ms. Denise Nichols

Basically, picking up on a few things that he said, we need a research central point so that we can get the word out to the veterans of what research is going on and if you need 50 patients, that we have a place to go to. For the doctors and researchers, we need the data on the web sites, on the web, of diagnosed illnesses, undiagnosed illnesses. You can code them, whatever you want to do to protect privacy, but this can be done. It would provide a lot of support and support is important, if you're talking -- everybody talks stress. Support 101 helps people, as we've shown in cardiac surgery and cancer, one on one support. These are things that need to be done that can be part of treatment. We need to have funds out here for the groups. We're working on shoestring budgets and helping people get the help, okay? I mean, shoestring. I have flight attendants that are donating [inaudible], we're taking care of some of the birth defect babies, these are some of the grass-root things that would help with what the scientists are doing.

The other thing is, that central web site has to be there. We're trying to get the word out to vets, but we don't have any phone money. There's not one of us that hasn't spent everything we have trying to help our fellow vets, and so we need it on the Internet and pull that material down. We can tell them, "Go to the library, it's up there, this is the address." We have a person working to try to get computers to vets so that they can interact with you. The web site needs to have feedback and question area to the researchers, because there is a fear. I was talking to a doctor back here just a few minutes ago. They're trying to do some treatments, but then there is a fear of the vet coming forward and saying, "I'm afraid to take this drug, I've already had problems." So, there needs to be a way that we can ask our questions publicly on the Internet.

We want to work together with you all. I just would encourage you, listen thoroughly, look at suggestions, get the testing. Like I said, the antibiotic testing. I live in Colorado and I've got vets out there. There's not a test site for antibiotics out there. And it's up to that VA hospital to volunteer. Well see, that's a control mechanism again. And with their budget being cut, they're doing all they can. There's some good VA people, but you have to have that access or provide travel for the vet to be involved in this, and this is what it's all about. It's us. So please, let's talk, come up to us, talk. We've been asking that to happen. Get our input. Thank you very much.

Dr. Benjamin Natelson, Chair

Thank you. And I think the idea of funds needed for broad recruitment base is obviously critical and I've listed that. Thank you.

Michael Woods
The Last Patrol
St. Cloud, Florida

I just want to take what Joe Poe said here and take it further. The VA must be mandated to do these tests on vets and it's not happening. I've been in the VA system for three years now and I've never been tested for depleted uranium, mycoplasma, having the SPECT scans done. If this group doesn't mandate the VA to run these tests, then it will not happen, and it will not ever get to the veteran, and we'll keep doing trials and research and everything else and ten years down the road, and myself, I still won't have had these tests. Are we going to get that on the board there?

Dr. Benjamin Natelson, Chair

I have it. Baseline . . .

Mr. Michael Woods

I see SPECT scans. I don't see mycoplasma.

Dr. Benjamin Natelson, Chair

Well, baseline data -- I put some for instances up there, I mean, obviously, what baseline data to be collected depends on the study.

Mr. Michael Woods

The studies are out there. The testing's been done, the research has been done. We've got everybody from every different group here. We need to be doing tests for them. You can't do a treatment until you have the answer on what the person's been exposed to. They need to be tested for every exposure that is known, that is a possibility.

Ann M. Maddrey, PhD
Assistant Professor
Director of Biobehavioral Programs
University of Texas Southwestern Medical Center

Dallas, Texas

I'm from UT Southwestern in Dallas and I am part of a major multi-disciplinary team which has been working in the last 12-18 months trying to get baselines in a number of areas from sleep, to SPECT, to MRI's, etc. And one of the things that we have moved to -- when I came to this conference, I thought that people were going to be talking about their treatment trials. We do have a treatment trial that we started back in October. It's an N of 1 trial, single blind, placebo controlled, randomized to treatment clinical trial. Let me explain that a little bit in regular terms. We have five medications that we have chosen to help in a variety of areas and what the patient does, there's a two-week baseline, and then they're randomized to a particular treatment. Each treatment is four weeks. There's a two-week placebo washout in between, and we do that for five drugs and a placebo period. So, this is controlled. It's been through our IRB, which is very difficult at the University of Texas, and let me tell you how it was based. It's based on an idea of "First, do no harm." And that's certainly what we don't want to do, but we want to help. We have chosen a cognitive enhancer because we feel that memory and all the cognitive symptoms are extremely important, an anxiolytic, a sleep medication, anti-depressant, beta blocker, and right now we are going back to our IRB to add on to the last phase of it the Modafinil drug, which is for narcolepsy, but it seems to have some promising results in other populations.

Touching on a few areas that Dr. Bascom had mentioned, the way we did this was in total collaboration with our veterans. We did this by asking, what the ten things were that they felt was most important to them, and what were the deficits that they might have. It might be not being able to drive, or interact with their family. So, what we did is, we have a number of outcome measures including the one that I just mentioned and standardized ones that we give our veterans that they send back to us every two weeks. In addition, and very importantly, I think, in terms of the education, we feel that the spouses have been left out of this process for a very long time, and the spouses are extremely integral to the process, both in terms of compliance with the medications for the veterans as well as for the need of being important. And the third reason is, sometimes when you have memory loss, you don't know it. That's one of the things about memory loss. You forget that you have it. With that, and irritability, you might be the only one who doesn't know that you're irritable. So, we've added the spouses in with a spouse caregiver survey that they fill out every month with the change of every drug.

That's basically the sum of our clinical trial. Short-term, I think that what was a very pilot study, we only have 17 veterans. We plan to do a much larger trial. In terms of the funding, this is my first Gulf War meeting and I didn't know all the politics that was going to happen here. But I do know this, we were going to do this treatment trial and the money was taken away because the DoD said that we cannot treat something that we don't know if it exists. So, that was my hearing of what happened.

Dr. Benjamin Natelson, Chair

Thanks very much for your input, Dr. Maddrey. Some of the panelists thought that Mr. Poe and Mr. Woods who had specific testing ideas and requests and thoughts, should be sure that your recommendations are heard at the Assessment Workshop, because for that workshop, testing is critically done. So, if you'd like to add your comments there, it might be doubly helpful.

Kyle Bitner
Regional Coordinator
ODSSA
Windsor Locks, Connecticut

I didn't know I was on this, but I do have something to say, so I'll go easy. Sir, first and foremost for you, I would like to yield my first portion of my moment to the panelist up there who had a question on the detox. You're cutting people off, there are answers that need to be given and understood. It must be nice to have an IRA or know what tomorrow's gonna be like. That's a benefit that you have that I don't. I would like an answer, and this gentleman to be able to ask his questions. You're cutting people off.

Dr. Benjamin Natelson, Chair

Well, I'm afraid there are many people . . .

Mr. Kyle Bitner

Sir, I'll tell you what, we can go longer and I'll talk to the head of the CDC to get this to happen.

Dr. Benjamin Natelson, Chair

Sir, your question?

Audience Member

The question I had was the excretion. You said 15% was through the sweat and 85% or so was through the GI tract. What do you measure as an outcome of success?

Dr. David Root

The measurement of outcome of success is how the patient feels after treatment rather than before. In terms of what we've done at my clinic, in terms of measuring what comes out in the urine, the feces and the sweat, we've done very little of that, because it's a private office, we don't have any funding for doing the more elegant testing, and that's what I think is going to need to be done. There has been considerable amount in the literature, however, and . . .

Audience Member

So the 15% and 85% is really kind of an estimate?

Dr. David Root

It's an estimate.

Dr. Benjamin Natelson, Chair

Thank you. Mr. Bitner.

Mr. Kyle Bitner

I yield the rest of my time.

Edward Bryan
Malden, Massachusetts

I'm just amazed at -- I'm totally disabled, both as a Gulf Veteran and a firefighter. It's just amazing that treatment is not taking place. No one's treating the Gulf veteran. They've got me on Prozac, Neurotin, Gabitril, Pentam, nothing else is taking place. No pulmonary function tests, they're not watching my lungs, they're not giving me any extra money for the chemical sensitivities, my wife and children are very upset with my actions and my activities. I have withdrawals from these medications. I'm trying to stay up on the self-medication and stuff like that. I'm trying to have a balance in there, and the VA, I go there for chest pains, because as a firefighter, they look at carbon monoxide as a heart attack in your muscles. It's not being addressed. The doctors have to go back to school. I think they've been out of school too long. They're not looking at the chemical exposures from the Gulf War, especially two chemicals, that I've researched very clearly and it's crude oil in the nerve agents that were underneath the oil wells.

What nerve agents they were, you'll have to contact the CIA and the Department of Defense. They know which chemicals were underneath those oil wells. They know. It's up to you people on this panel to find out for us so that we can get the proper treatment. They won't even see me in the VA anymore. I have to go outside. I have to use my social security and go outside the VA for my care. It's sad. When is the treatment going to start? When? I want to know when. Can any panelist member up there tell me when it's going to start? These Gulf veterans are waiting for treatment . They're suffering dearly. They need help. And they need a lot more than the care that they've been getting. They throw you out of the VA. They don't hold on to you anymore. They put you in nursing homes. Alzheimer's disease is going to be a big factor out of this, a big,

big factor, and ALS. Can any of the members up there tell me when the treatment's going to start, or get the VA to start bringing the veterans in for 100% recall? That's what I'm looking for, 100% recall. Can anybody answer that?

Dr. Benjamin Natelson, Chair

Thank you, Mr. Bryan. Of course the purpose of this panel is to try to come up with concrete answers as to new trials.

C. Kirt Love
Signing My Life Away
Copperas Cove, Texas

I served during Desert Shield/Desert Storm. In my community, the VA doesn't do a lot of outreach. The thing is that they see one Gulf War vet a week. And what they've told me and others is to try to bring them in. I can't bring them in because these vets tell me the same thing – they're tired of being treated like garbage. They've gone in and been told they're not sick, they've been told they're hypochondriacs, and they get to the point where they don't want to come in because they feel they're being lied to. Not all, but many of them that I'm talking with. I've got one individual that was drawing about $900 a month. He's been reduced to $150 a month. He can't take care of himself, he's on morphine, he's got real serious problems and when I go back, I don't have anything positive to tell him at this point.

What will be implemented this year? I hear two, three years? I hear other things that are going to happen. I'm one of those suffering myself. What have I got to look forward to when I go back? I don't have a job waiting for me, there's nothing secured, there's no family – there's no such thing as dating when you're sick. People don't want to be around you. My family stays away from me because I'm sick. My friends stay away from me because I'm sick. I'm isolated. Gulf War syndrome is a joke in our community. You don't talk about it because people chuckle when they hear about Gulf War syndrome. I'm generally treated with disrespect from the community that I live in. And it is very difficult to get this information out, get it rallied. The media is not interested because it is treated as a joke. Even with Gulf War vets serving as camera people, they don't even want to address this. They're so burnt out themselves, they don't even want to talk about it. There's other things that come up.

One of the things that I'm curious about, I received the IgG when I deployed. These vaccines, huge needles, huge volumes of this material that's refrigerated -- I have people coming up with hepatitis and other things, approaching me. I've talked with thousands of vets, and I get lots of them coming up with autoimmune disorders. I find other things going back to autoimmune, autoimmune, autoimmune. The IgG, the IgA, the contaminated blood products that were used to supply this, the shortage at the time, the extreme expense of these shots, I hear mention of

squalene and other additives that are used in HIV research that tie back to gamma globulin. And I'm really terribly curious about the gamma globulin shots. If we've got so many people turning up with these types of autoimmune disorders, and yet, these individuals are summarily dismissed, because this is not part of the regimented program, this is something a little bit on the edge.

For me, I believe that Gulf War problems are a variety of problems and that's why the illness varies from person to person, because of the variety. So, I'd like to see a little bit more research done in areas of immune and I'd like to hear more about this enzyme antibody-based program that they were implementing during the Gulf War. I hear an awful lot about the enzyme restrictors and other types of materials. There's an awful lot of autoimmune research that I think is being dismissed. I yield the floor.

Dr. Benjamin Natelson, Chair

Thank you. The next person.

Audience Member

Excuse me. You cut off Joe Poe earlier and I would like, and our vets back here would like Joe to finish up what he had to say.

Dr. Benjamin Natelson, Chair

Excuse me. My task is not an easy one. Four minutes for each speaker. I have to get through this list to give every one his and her chance.

Donald Edwards
Special Projects Coordinator
for Congressman Sanders
Burlington, Vermont

I want to say as Congressman Sanders' representative that I think this is reprehensible. You've got a vet here that wants to speak. I think you ought to hear him.

Dr. Benjamin Natelson, Chair

If we have time after everyone else, we'll give him more time, Mr. Edwards. We have four minutes for each person.

Audience Member

Sir, the man has speech difficulties. You should allow a little bit more time for disabilities. We have a disability act in this country.

Dr. Benjamin Natelson, Chair

Fine. We'll try to give him another two minutes after everyone on the list is done. Go ahead, madame.

Audience Member

I would like to see research done on using neurological chiropractors who use kinesiology and nutrition to treat these chemical sensitivities. And also, I'd like to see research done on the aspartame disease. The research that I have on this says that when the temperature of aspartame exceeds 86 degrees Fahrenheit, the wood alcohol in aspartame converts to formaldehyde and then to formic acid, which in turn, causes metabolic acidosis. Formic acid is the poison found in the sting of fire ants. The methanol toxicity mimics multiple sclerosis, thus people were being diagnosed with MS in error. The MS is not a death sentence, but methanol toxicity is. And it says that the cause behind some of the mystery of the Desert Storm health problems -- they have the burning tongue and other problems, discussed in over six direct cases can be directly related to the consumption of aspartame products. Several thousand pallets of diet drinks were shipped to the Desert Storm troops. Remember, we can liberate the methanol from the aspartame at 86 degrees. Diet drinks sat in 120 degree Fahrenheit Arabian sun for weeks at a time on pallets. The service men and women drank them all day long. All their symptoms are identical to aspartame poisoning.

Dr. Benjamin Natelson, Chair

Thank you. Mr. Poe, do you want to come back now and give us another few minutes to complete your remarks?

Mr. Joseph Poe

I'm looking, Sir, at ways of saving time and money and efforts. Maybe I was in the wrong place. You said "assessment." But you can't – where do treatment and assessment separate, Sir? I do not know that. Without the right test, you cannot do the right treatment. Without the right treatment, you do not know what the next test is to do. With the SPECT guide, it allows the cutting of time. This is still treatment, right, Sir? You're a doctor, you're a researcher, you're doing something for your patient in treatment. You do not want to use a useless test. We have these people, it doesn't matter whether they're veterans or not, that use these tests. Somebody help me out. I don't want to go past two minutes, okay?

Dr. Benjamin Natelson, Chair

Go right ahead. Finish this four minutes.

Mr. Joseph Poe

The MRI debate -- there's people that believe that there is a possibility our problems were created by MRI. I do not believe that is the answer. I do know I am double positive for it and do not know where it came from. There are people that believe it is only DU. I do not believe that. But I do believe that they should be tested for the DU, Sir. Now, that's were I'm coming from -- baseline. Now, if you're testing for that baseline across the board, and in a situation which covers errors where nobody has to worry about what goes into the newspapers, this is treating, because you're getting the test done and you know what kind of medicines to do or not do, and you're not wasting more time. Nobody is. And nobody loses face. DoD does not get cursed, VA does not get cursed, CDC does not get cursed. It's a pretty simple thing and I will not say anymore because you're fidgeting and you want me to move on, so I'm going to.

Dr. Stuart Brooks

I'm just trying to understand the point that you're trying to make. Is it that you think we or the VA facility should be utilizing all of the tests that are currently available for diagnosis as a baseline or for some specific types of tests that need to be done?

Mr. Joseph Poe

I think it's crazy to run 100 or 2,000 tests or whatever for everything, for baseline. That's not what I'm saying. I'm saying there's really three or four primary things that have been dealt with for eight years here. And that is depleted uranium, which is very powerful in itself, and I'm not talking about naturally occurring uranium. We're talking about weapons, created from nuclear waste. That is the trick. Big difference between that and natural occurring uranium. Now, this has been up there, it's been put out 300 times, okay, in the air and all that. Whether depleted uranium is bothering me or not, is moot. Whether it is doing a bad deed to another is not moot. Now, the major issues that you hear over and over again is the media is one of the problems. You can't treat the media . . .

Dr. Benjamin Natelson, Chair

Mr. Poe, can you finish up because we have several other speakers.

Mr. Joseph Poe

I sure can. Does that help, Sir?

Dr. Stuart Brooks

So, depleted uranium is a concern. Is there any other specific . . .

Mr. Joseph Poe

Yes, mycoplasma fermentans, incognitus. We are not talking about natural mycoplasmas. We're talking about laboratory-altered, and that is verified, and the CDC does know that is verified. So I don't have to go further with that.

Dr. Rebecca Bascom

He said there were four things. One was DU, one was altered mycoplasma. What was number three and number four?

Mr. Joseph Poe

The SPECT scan was for the neurologies. Now that helps everybody, whether veteran or not because of its view into the brain, and you can go on into doing many things.

Dr. Benjamin Natelson, Chair

And the fourth?

Mr. Joseph Poe

Good God, Sir, I forget now. The fourth is, a lot of times part of treatment is not doing treatment that is worthless.

Dr. Benjamin Natelson, Chair

Thank you, Mr. Poe. The next person on the list is Marc Zolre. Is Marc Zolre here? The next person on the list is Don Salisbury.

Audience Member

Are you going to list those things that Mr. Poe mentioned on the . . .

Dr. Benjamin Natelson, Chair

The difficulty is -- our panelists have written it down. We need treatment suggestions and I'm not exactly sure, I mean, these are concerns, I know the mycoplasma treatment is out there for it, so we need treatment suggestions. The panelists hear the concerns. I'd like to task them -- we're coming up with some treatment suggestions.

Dr. Rebecca Bascom

Dr. Brooks and I and Dr. Fiedler are tasked with the macro view, which means the big picture, that includes the big lists that need to be included. Other subgroups, Dr. Natelson has charged with doing more specific lists of specific therapies. We're busily writing over here.

Don Salisbury, DO
Gulf War Clinic Medical Director
Albuquerque VA Medical Center
Albuquerque, New Mexico

I'm with the Albuquerque VA, and I am the medical director of our Gulf War treatment program, and we have a clinic that is dedicated to and for Gulf War veterans. Mr. Poe, I want to thank you and Denise. I want to thank you for your comments, and anybody from Colorado who can get to Albuquerque, please come down because we're going to be participating in both the antibiotic trial and the cognitive behavioral therapy trial. And I think it's great, we have to get the word out, and anything you can think of to get the word out, we'd appreciate it. So, Albuquerque's on the map. We're doing DU testing, we're doing any testing that's necessary. We're a tertiary care medical care center, we're affiliated with the University of New Mexico, and all of these are available through us, and more. And treatment too. We're testing for uranium through Melissa McDiarmid's program in Baltimore.

Audience Member

But she's never had any positive findings.

Dr. Don Salisbury

She has had positive findings. She's following the veterans that have had higher than baseline values, the friendly fire incidents, etc. We don't have SPECT scan availability, but I can answer any other questions you have out in the hallway, because I only have four minutes and I want to talk about my other thing.

I wanted to propose, and I hope it's not taken like the finger painting issues and things like that, because this is a little different and it's alternative medicine and it's on the back of the envelope. As we sat here discussing this, my father-in-law would never forgive me if I didn't bring this up,

he's an acupuncturist. They have what they call median regulatory acupuncture, MRA. This is a unique form of acupuncture, it's not the traditional acupuncture, it's more of a Western form. It's electronic and it's scientific. We find that it's safe. It's used in childbirth, it's not detrimental to the veteran, it wouldn't be detrimental to anybody that uses it. It has objective and reproducible criteria for diagnostic purposes as well as therapeutic and treatment purposes. I think that we could definitely show both symptom improvement and improvement in balancing the meridians as we talk about in acupuncture. And in the Gulf War veterans, we can show there is an imbalance in the meridians. It's certainly not a Western concept, but it blends Western and Eastern medicine together. And I'd like to propose that this form of acupuncture be addressed. And I know our Chairman, Dr. Natelson, mentioned acupuncture initially in the introduction, so I felt encouraged to bring it up. It's not too far afield anymore, with NIH actually finding that it does have, especially in pain relief, a real place in our armoratorium of treatment options. I would hope that we could consider this, and if the committee would like to talk to me later about this, I would love to give you more information. But as I said, it's just the back of an envelope. Thank you.

Vinh Cam, PhD
Presidential Special Oversight Board
for DOD Investigations of Gulf War
Chemical and Biological Incidents
Greenwich, Connecticut

I'm a member of the Presidential Special Oversight Board for the Department of Defense's investigations of Gulf War chemical and biological incidents. I have four recommendations. My first point is to develop human immunotoxicity tests for patients. I'm very glad that the lady before me stressed the importance of the human studies. My second recommendation is to standardize the tests you have developed, so that there is consistency among all institutions and researchers working on this issue. It's very important, I can't stress enough, a quality database, so make sure that whichever indicator test you use, make sure they are reproducible.

My second point is in designing clinical trials, it is very important to use the set of immunotoxicity tests that you have developed, use that for pre- and post-treatment so that we have points of comparison. Also, it's important to develop very clear criteria in choosing the patient group and the control group, so that in the future, if other researchers want to do another experiment, amplify this kind of research, there is a very clear guideline. And again, the ultimate goal is to create a quality database.

My third point is, use experimental drugs, if possible. I know some patients would love to but they just don't have the political clout to do it, but CDC might be able to do that, I hope.

My fourth point is outreach. It was not the first time I heard all the concerns I heard today. It is important for us not to lose focus that these clinical trials are for Gulf War patients and time is

running out. So do the best. You can't have every possible person that you want, and also maybe you could categorize. These are the kind of surveys or tests they could respond to.

My point is, I feel that the leadership of DoD and VA really want the programs to work, but there are a lot of operational issues that need to be ironed out. And this requires tremendous effort in coordinating everybody in the loop, including delivering the message out to the Gulf War community. Thank you.

Dr. Benjamin Natelson, Chair

I think the one concrete response to this, and I mentioned it yesterday, there is a trial of the immunoactive material called ampligen, a mismatched RNA, which a company called Hemispherix has had approved for patients who fulfill the case definition of chronic fatigue syndrome. They also have a cost recovery program which costs the patient $15,000 a year, which is obviously a problem, but if any veteran with chronic fatigue syndrome is near any of the sites that are doing this, it's twice a week infusions of an immune active material, they should partake in it. I know the various sites are always looking for patients, so that's available. Chuck, you had a question and I wanted to make sure that everyone is heard, so please, now it's time for the panel to ask questions to the individuals who spoke, to try to shape some recommendations.

LTC Charles Engel

I really just wanted to bail you out, Ben, and say that the suggestion to also present some of the testing at the Assessment seminar was my own. That isn't because we don't want to offer it as clinical care or treatment, but more just to give you another opportunity to have those recommendations heard, and I regret it that came across as we weren't interested in that, because I think that we are very interested in testing as a part of clinical care.

Dr. Vinh Cam

I didn't mean that you weren't interested. What I was trying to say is just to have logic and senses and it would be easier for people to do those kinds of testing. Because I know there is a lot of compliance issues you have to follow.

Dr. Benjamin Natelson, Chair

Well, obviously. One of the things I asked us not to focus on, because it was so difficult, but the point that I think Mr. Poe raised is, I think you need to know what you're treating. Obviously, you are not going to design an immunotherapy for some non-immunological because of an ailment. So obviously, this is the bread and butter of any clinical trial, that appropriate testing be done, that it be used as a dependent variable for outcome. So, I think that we all agree with that.

Dr. Rebecca Bascom

For many cooperative trials, a data coordinating center is a very key part of the organization. That is a group that knows how to make sure that data is good, knows how to analyze it, and is pulling it all together. I wondered if, when you were suggesting the importance of a) coordination, b) quality of testing and c) the ability to look for different groups of people, some who are very sick and some who had a different pattern, that a data coordinating center that brought together, for example, Dr. Maddrey's outcome measures and used them around the country, that that could fulfill some of your requirements so that instead of thinking of this as a bunch of little trials that people put in for, really have a Gulf War or veterans' clinical treatment network with a data coordinating center and to move ahead in that coordinated fashion.

Dr. Vinh Cam

Well, I'm glad that's being done, and my wish is to see that sustained.

Dr. Rebecca Bascom

No, I'm not saying it's being done. I'm saying as I listened to what you're saying, and as I listened to what Dr. Maddrey said, and as I listen to all the Vets, I'm thinking that that's what's emerging in my mind as the macro piece and I'm wondering if that makes sense to you.

Dr. Vinh Cam

Yes, it does.

Dr. Benjamin Natelson, Chair

I think that's a great concept. Can you give me a one-liner that I can use?

Dr. Rebecca Bascom

So, it's a Gulf War treatment network with the purpose of doing clinical trials that has a central data coordinating center, that has oversight input by veterans and other interested groups, and at the steering committee level, that is a point of contact for experimental drugs that people hear about, and that this group can make the decision on stratification and who should get something that's way out there, may have high risk, but who's got the kind of condition for which that's a reasonable risk benefit.

Dr. Benjamin Natelson, Chair

That's really helpful. That's great. That really integrated a lot of the ideas and would certainly respond to the things we've heard from some of the veterans, with the need to get some of the input.

Ms. Wendy Wendler

Can we clarify some of the things that she meant? I'm with you. Mrs. Whitcomb spoke last night. Her son may be in four or five different studies. So right now, we're already doing it literally, and if Jason Whitcomb is in four studies and goes to Philadelphia, and Dallas, and the VA, and here, and he's in the protocols, and he's screened, is there going to be some sort of cross reference among the researchers? From the patient up and from the researcher down?

Dr. Rebecca Bascom

Yes. What I'm saying is, it needs to meet in the middle. In asthma, for example, they've been doing this for the last few years and it means that the people with the best ideas in terms of treatment, they get together and they brainstorm and then they go home and talk to their patients, and then they get together and they brainstorm. But there's a central place where people are making sure that the records are being kept and the records are kept clean, because a lot of times the people who are really good at dreaming up ideas are not so good at keeping the records straight or the details. So, what you do is you make one detail center, and they take care of the details and make sure the quality is good.

Ms. Wendy Wendler

It's sort of a military model in the sense that the Army, Navy, Air Force all has to take this island and we're going to make sure we all know what they're doing and nobody bombs each other. One more point I would like to make is that in the analysis of following it, for instance, is there a way to rule out some things it's not? Somehow we find out where we're going by not going where we don't have to do. Particularly with the antibiotic concerns. I work with geriatric models a lot, and you know that if someone has diabetes and tuberculosis and is getting a hip replacement, you can't say we'll take it one step at a time. Just because he's having hip surgery doesn't mean he doesn't need his insulin. And I guess I'm still concerned that the researchers are focusing in on their particular study and it needs to be narrowed and blah, blah, blah. But whether they're getting enough B-complex to be able to answer your questions and make sense, whether or not they're screened down and don't have the strep, I mean, Dr. Hyman is not treating anyone who does not have the strep. But if you're going to treat anyone with an antibiotic and doxycycline doesn't work on strep, you're not going to be able to say which antibiotic is killing which bug, unless you at least, pre-screen. That's what Joe Poe's remark about this baseline might just be ruling out some things, we don't have to worry about that, but they're not cluttering up studies, with Jason Whitcom being screened by all these different people.

Dr. Rebecca Bascom

One of the things I've taken from listening over the last couple of days, is that there is a group of people in the category of unexplained illnesses, that's what it's being called the 1,500 or so that don't fit an easy box. And that, in itself, could be a cohort group, meaning, okay, Joe, I think it was you who said, "Think of everybody together. Think of those 1,500." And the task could be: Is there any way to improve the health status of those 1,500 people?

Ms. Wendy Wendler

And remember, the label of "undiagnosed" is merely that. I'm the English major. It's just because the VA or somebody has said they're undiagnosed. And if somebody else has already found something in Jason because he had a Medicare card, the Medicare card couldn't get him that information, whoever else had him in his study should at least know enough medical history, whatever, from all sources. I'm not sure "undiagnosed" is the . . .

Dr. Rebecca Bascom

I'm using "undiagnosed" just as a way to identify a group of people. I think, we all think, we need to know more about how to be able to move them forward with their lives.

Ms. Wendy Wendler

Since 1993, we've been calling them the "point walker" cases. It's because, well, I'm trying to de-genderfy the word point man. In the military the point man is out in front and they're protecting the squad behind them. It's an arrow-shaped formation. We just think the "point walker" cases would be this cross-pollinating, this cross-referencing way to describe them. I know you all think "random" is part of this epidemiology, but, sometimes if you pick a case on purpose, even if it's somebody's son or whoever, it's not meant to be personal, but it's just because they're the perfect canary for this particular mine.

Dr. Rebecca Bascom

I want to just say one thing about that. I think that the studies that have been done over the last number of years, the mortality studies, the big-picture studies, those are important kinds of studies but it's a different philosophy. You're asking a different question, so you go about it differently. When you're doing a treatment study, you start with the hurting person and try to move them from hurting to not hurting. And that involves, trying to. . . if the hypothesis is they're hurting because it's an infection, but we don't know, but it might be, that's why we do the mycoplasma. Or we say, neurologically, maybe it's a median electrical field deregulation, so let's try to intervene with that. But the point is, it's not based on service to the Gulf, it's based on hurting.

Ms. Wendy Wendler

Well, maybe we're both saying the same thing but, I'm just using Jason as an example because I know it better than others. He blew up the bunkers at Khamisiyah. If we're going to pick some of the people and pick exposures, but he also has to be on the mycoplasma and the strep. We use the phrases inherently problematical, military lifestyle and workplace. This is such a unique situation, that maybe we need to sort of adjust some of the typical peer review criteria to just say we're going to learn a lot from certain people who just happen to be involved in certain things and we're not showing them preference over another vet.

Dr. Rebecca Bascom

I think it was the firefighter that was talking, who reminded me of a real wise man who once said, "If you're trying to help, you look for the fire and you put out the fire." And that's what you do first. You don't look for every little spec of charcoal that you find warm.

Ms. Wendy Wendler

Well, Denise is an Air Force nurse, and if someone comes into the ER bleeding from a head wound, whether they were hit in the head by a 2 X 4 or a baseball bat does not matter in her particular position. It will matter to a prosecutor and a defense attorney in a courtroom six months later – who mugged the guy. And one of our concerns is that we're taking too long to do this and we can do some of these steps at the same time. But I'll tell you what, I was exposed to Agent Blue, cacodylic acid, which the Air Force chooses to call Agent Blue because they didn't want to tell anybody that arsenic was in it, because even my mamma who saw Cary Grant in *Arsenic and Old Lace*, knows arsenic is not fun. Cacodylic acid? Who knows? So, I'm just saying, I've been there, done that.

In 1984, I testified in Judge Weinstein's committee on Agent Orange. We're saying the same things about many of the same chemistries. There are enough experts in the veteran community, I'll just say this, to tell you all how to do this, but you need to give us more than five minutes. Give us a forum. I will say DSGF is going to prepare some more written materials for you, and I'm sorry, I feel real inarticulate this morning, but . . .

Dr. Dan Clauw

I just wanted everyone to, especially people on the panel, to understand a couple of things about the trials that are going to begin in the next couple of months. First of all, those are for the patients that I think all of us are talking about. People who are – who don't have established diagnoses and have symptoms such as pain, fatigue, memory problems and things like that. So, individuals who don't have an established diagnosis or have been undiagnosed or people who

have been labeled with diagnoses that might not quite explain their symptoms will be eligible for those trials. The antibiotic trial will do the mycoplasma testing and those individuals who test positive will be randomized, to either receive antibiotics or receive placebo, and the other trial, the exercise and cognitive behavioral therapy trial, will be to all-comers. There won't be any entry criteria other than that people are symptomatic.

The other thing, Becky that you were speaking to, is the only reason that I became involved in this exercise in cognitive behavioral therapy trial was the opportunity to work with the VA cooperative trials network. It is, without question, the best cooperative trials network in the world. It has been responsible for nearly all of the large, multi-center studies in coronary artery disease, and lipids and hypertension, stuff like that. The VA has a tremendous, there are some things the VA does extremely well and some things that they don't do very well, and I think we all know that, but it's a tremendous resource and I think that is what's going to be used for any of the trials that are going to occur. The coordinating centers handle the data analysis, the data entry, the outcome criteria, the statistical analysis, that as you say, some of us who might be able to come up with good ideas, maybe aren't as good at the day to day details. So again, it's a tremendous resource and I think that any of the trials that are likely to be done will somehow be coordinated through this VA cooperative trials network.

Dr. Rebecca Bascom

Well, I think the question is, given the history, if the VA center, is the place to do it, or the CDC is the place to set up the coordinating center, and I think that discussion is something that Congressman Sanders and the CDC and the VA need to all have together to make sure they are all comfortable with the quality of the data coordinating center. But I have to tell you, when I was in med school, and I was at the Oregon VA and I had my first couple of patients that had lung cancer and that were telling me stories of World War II, they knew what they should do about their high blood pressure because of a VA cooperative study that had been done. And the reason that some of us that have parents who aren't stroking out right now, is because of a VA study.

Ms. Denise Nichols

One of the important things, some of these vets haven't gotten the testing diagnosis in order to get the treatment. There's horror stories out there, galore. When I have patients who come in with chest pains and they don't get an EKG, excuse me, that's one thing that I was taught, I had a cardiovascular specialty, get them on an EKG. We have other stories here of vets who went to the VA, tried to get things done, come to find out -- Kyle has a cancer in the spinal chord. He wasn't diagnosed. We need some kind of review board to be putting these problems into, to get these problems solved so they aren't so wide-based all across the country. Kyle's not the only one, there's been others. We've had to go to civilian doctors. Besides the treatment trials, we

need some kind of other coordination with the civilian doctors out there. That's where we're having to go and I've been calling doctors that I knew way back when, active duty, that are civilian, and asking for their help. So, some of the communication is not just to the vet, it's to the doctors. Gil Roman, who hasn't come in yet, Gil has problems with cardiac. He's scheduled for open heart surgery. And he has been able to use chelation therapy which has helped him. He's done it, what, about 32 times? It's lowered his cholesterol levels, so it's not hurting him. And it was through a civilian doctor out in Colorado. And it's similar to the Root therapy and some other people who are doing it out in California and various places. And one of the things I found out from Barry Walker this is part of the networking that we do, Barry Walker had cardiac problems, and he had a good VA doctor that was dealing with the cardiac problems, that was networking. We need these people identified for other VA centers, and praise them and not fire them, if I heard that right, Wendy. Because they're trying to coordinate and they're trying to help us.

But remember, if you don't test them, you know, like we've had autoimmune-type disorders, I haven't gotten all the testing for autoimmune, so maybe I could be diagnosed. You know, it might be another diagnosis besides my thyroid and other things, but you've got to test them before the treatment, and if vets are having to go to civilian doctors and other resources, something is terribly wrong here. And you can't even get to the treatment because you haven't got a diagnosis. Thank you.

Dr. Benjamin Natelson, Chair

Very good. I think everyone has, we've achieved something quite remarkable here.

Dr. Leslie Israel

Well, basically what's being addressed is quality care, and we know the VA system has some of the best physicians in the world associated with prominent medical schools, and they're also places where they have poorly trained, not so good physicians and people from other countries maybe don't meet the standards of the civilian population, and what we really need is a way for veterans who aren't satisfied with their care to escape somewhere else, whether it's the VA center associated with the major medical center that has top physicians or to go into the private practice realm. That probably should be addressed in the Macro group.

Dr. Benjamin Natelson, Chair

Thank you. Well, I think that's an issue. Well, my goal was to try let everyone be heard and I apologize if I stepped on any toes while doing it, but I think everyone was heard, which is pretty remarkable. Now, for the people in the audience, these are our current -- again, I am being tasked to come up with some kind of report. If anyone in the audience wants to input further, I'm going

to ask if the panel can stick around another five minutes. I have to go meet with the other workshop leaders so that we know what's happening with assessment vis a vis this testing and diagnosis so that we have some input. So just come with your groups. I need to task the workshop members to do the following thing, because we're going to come together at 3:15 and in order to be somewhere by 5:30, I need concrete one-line ideas from each workshop member.

What I figure is, if there are 13 of us on the workshop, 13 short-term, how can we respond to a number of veterans who said I don't want to wait a year or two, how can I get something now? So, we're going to try to be as short-term as we could possibly be. And then, long-term. What would be the long-term benefit in each of our plans? So, I'm looking for two brief lines from every person, short and long term and then we'll compress that further, because 26 lines might be too long from one workshop. So that will be the work we will do in the afternoon workshop session. So, members of the audience, interact now with members of the panel so that we can be sure to get your comments going. Thank you for your help. Thank you.

The session was adjourned.

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Day 2 – Monday, March 1, 1999 - Afternoon Session

Dr. Benjamin Natelson, Chair

So, what I've done is, I've sort of ignored the clock. What I'd like to do is say that in two minutes, I stop ignoring the clock and we get started. We're short one workgroup session unless we start putting our heads together. So, we've got two minutes of caucusing. Now, if we do not have consensus, that's okay. What I'd like to do is see where the workshop is and get some ideas written down, so let's get started on the easy one, which is our section on pharmaceuticals, including homeopathics, vitamins and minerals. What I'm going to do is, I will write on the plastic sheets where we are, and then we'll try and discuss each one as it comes. So, the first one then, is going to be "pharmaceutical," and I've asked Dan to be the Spokesperson. The first is short-term.

Dr. Dan Clauw

Two recommendations with respect to short-term studies were to consider doing Pharmacologic studies that would address management of idiopathic symptoms such as pain and fatigue, since these are such prominent components of these illnesses. I'm sorry, cognitive dysfunction and pain. The drugs that we found were most promising for treating pain were low doses of tricyclic drugs, venlafaxine which is Effexor, and Ultram, which is tramadol.

Dr. Benjamin Natelson, Chair

And the idea here, if I may, is that we would do an assessment here, which would be quality of life, pain and symptoms. And this would be what we call an "open label." Does the low-dose tricyclic (TCA) help the veteran? And we would assess here, and we would assess here, and then finally here. So, it's not controlled, but we are collecting data, and I think one thing we would like to do is, are any of the veterans here? Good. One of the things that we want to be responded to, is whether you think we're helping you. So, aside from quality of life, we're going to ask you this sort of business question: Are you satisfied? I would do that. I would rather have a satisfied than a non-satisfied veteran. So this would be the plan, very short-term, easily put into motion. You have pain, here's a protocol.

Some veteran was asking about whether he or she could use such a protocol with his or her private doctor, and the answer is, of course. They may not need to collect the data, but they could sure try it.

LTC Charles Engel

Another idea for a global assessment question would be: "Do you feel that this medicine is helping

you?"

Dr. Benjamin Natelson, Chair

Alright, let me do this again. That's TCA, then it's, that's tricyclics, sorry, for the abbreviation, then the drug Effexor, and each arrow is a probe, then Ultram which is a pain reliever but a non-narcotic. Okay, so please, Chuck, what would you call the questions that you're . . .

LTC Charles Engel

It's sort of a global efficacy question: "Do you feel this medicine is helping you?"

Dr. Benjamin Natelson, Chair

Alright, good. Quality of life, I thought would be good, a pain, an overall symptom checklist, and then the last would be satisfaction. So, I mean, if you did this on 30 veterans who were ill . . .

Ms. Wendy Wendler

Are those the only three pain medications suggested?

Dr. Benjamin Natelson, Chair

What we're trying to do is come up with a trial, and we put our heads together and what, if you were a treating doctor, and someone came in to you with unexplained pain, what would you do? The thing is, doctors do this without testing it.

Ms. Wendy Wendler

We have three that have worked very well that are not up there. Glucosamine chondroitin -- it's a natural joint pain reliever, it seems to work miracles, repeatedly, I've seen it again and again. It starts to kick in, in about three to four weeks or sooner, vitamin B1, thiamin -- the special forces medics would use . . .

Dr. Dan Clauw

We're going to talk about nutritional supplements in a minute here, so if these are. . .

Ms. Wendy Wendler

Thiamin, sometimes they would use an injection here, but it seems like that would have to be monitored. The thiamin and B1 shots that are used professionally for alcoholism, and the medics in Southeast Asia and the refugee camps, since this was injection, have to be doctor monitored, and the methadone that the VA is using, I know deals with a lot of opiate receptor problems, but the methadone has really helped some of my worst vets that I work with.

Dr. Benjamin Natelson, Chair

Let me try to tell you how I, as a researcher would deal with that. The chondroitin, this is the first time that I have ever heard of that, so, that's my problem, I admit, but I don't know if -- do you . . .

Dr. Dan Clauw

Yes, I'm a rheumatologist, so we get asked about chondroitins about 20 times a day. What chondroitins, what glucosamine chondroitin sulfates have been shown to be successful for is osteoarthritis. They haven't been shown to be effective for pain for non-arthritic conditions. And again, I think we're going to talk -- and if we have do deal with every individual's medication that they have, we'll never get done. We're going to talk more globally about nutritional supplements in a minute and hopefully, what we have, you'll be happy with.

Dr. Benjamin Natelson, Chair

Again, I was unaware of B1 as a treatment for chronic pain. We use B6 for headaches certainly, and we all agree there is a role for opiates, but this would be a step -- obviously getting these data on Gulf War veterans with unexplained pain would surely help every practitioner. Wouldn't you like these data, Dr. Gordon, in your practice?

Dr. Frederick Petty

If I could just suggest, rather than TCA, you make that more specific, like doxepin, for example, which I think is a very good drug. I use that a lot and also, I would suggest inserting in the beginning, a brief screen for possible bi-polar disorder, which we have one, you're welcome to use. It's like a little one-page checklist that can be self administered, just to make sure you don't make their condition worse.

Dr. Benjamin Natelson, Chair

If we could move on now to a short term for cognitive, Dr. Clauw.

Dr. Dan Clauw

Consider a similar type of trial treating the symptom of cognitive dysfunction and this could include medications such as pemoline, which is Cylert, and/or Wellbutrin.

Dr. Benjamin Natelson, Chair

Now I would push in such a thing where it's one or the other, that that be at least, single blind placebo controlled, because here, to get placebo is very complicated. But here, when it's one or the other, I would push for placebo so that we could learn the discreet effect.

Dr. William Baumzweiger

The recent studies show that Cylert is totally useless. It just doesn't work in any form of neuro-cognitive improvement. Wellbutrin much better. I would actually try something like one of the new Alzheimer's drugs if you're going to go that route.

Dr. Benjamin Natelson, Chair

See, I've always been very negative on that. That's a specific cholinomimetic hypothesis. Of course, there is a galantamine trial which is a cholinomimetic. The reason the Alzheimer people are using cholinomimetics is that the cholinergic nervous system is low in the ailment. We don't know anything about the cholinergic nervous system in unexplained illness, even in subsets like chronic fatigue.

Dr. William Baumzweiger

But we know a big component was nerve gas which attacks the cholinergic system specifically, and so you have to assume there's some damage to it.

Dr. Benjamin Natelson, Chair

Well, you can assume that, but you'd have difficulty assuming which system is involved. To me, that's less evidence-based.

Panel Member

What about assessment, some kind of assessment effort before?

Dr. Benjamin Natelson, Chair

Well, you could do brain cholinergic assessments with PET, but that's not what we're about.

That's the other workshop. That's been used in Alzheimer to assess cholinergic factors in Alzheimer -- well, I will put it down.

Panel Member

I noticed that the medications you do have up there, Cylert and Wellbutrin are dopaminergic agents, and yet we don't have any information that the Gulf vets have any dopaminergic problem. My point is, if we don't have information for that and we don't have information for the cholinergic problem, what makes those two different?

Dr. Benjamin Natelson, Chair

Well, we do have some anecdotal data that this doctor and this doctor have used and feel it has, I mean, I've used Wellbutrin and not been impressed by it as a cognitive enhancer. They are, that's a trial. I mean, this is a cognitive enhancer in Alzheimer's, and to try it in Gulf War illness, to me, that's a big leap. It's less evidence driven. I would not do that study with my own sweat, because it could turn out to be, you know, the probability of a negative study is reasonably high. I mean, I'll put it down if people think it's worth doing. [Audience agrees to include it.] And again, it's placebo controlled, we'll figure it out. [Audience continues to discuss different drug treatments.]

Dr. Ann Maddrey

I mentioned earlier that we are doing a clinical trial right now and for cognitive dysfunction we are using Aricept. I have no idea whether it's working, but our trial will be finished at the beginning of June and we would certainly like replication of the data or, and I'm sure this isn't going to be ready by the middle of June, but if it doesn't work, we could absolutely say that, so that's in terms of the cognitive enhancer.

I do think that you're going to have trouble with defining pain as a uni-dimensional approach right now, because the Gulf War veterans that I have talked to and that are on our protocol, it would be difficult to just treat them for pain because there are so many areas of the body involved. The other thing is, when you talk about questionnaires, what kind of data you're going to collect, we collect data every two weeks, five different outcome measures and one of the things that we have learned that we can't do, is just ask people how they are, or if they are satisfied with the treatment, or: "Does this medicine make you better?" Because what that question elicits is, I don't know if it's the medicine, I don't know if it's the cycle of the illness, I don't know a lot of variables, so I would be far more specific in doing drug trials in terms of your outcome measures.

Dr. Benjamin Natelson, Chair

I think you're right. What I tried to do with my colleagues is to pick areas that you'd like to assess. I don't think we came up with the actual vehicles. And the question of what vehicles would be, again, we're trying to give a one-liner here. So, I think your comment is extremely well-taken, you have to pick your vehicles more carefully, but the sorts of things we were talking about, quality of life, veteran satisfaction -- Do you have a problem with them?

Dr. Ann Maddrey

No, I certainly do not. One item that I would think to include in terms of cognitive dysfunction is an item that is not that well known. It's called the Neuropsychological Impairment Scale, the NIS. It's a self-report measure and we've found that it has been excellent in discriminating cases from controls and we hope that it's also going to be excellent in our clinical trial.

Jim Binns, BA
Chairman
Parallel Design
Phoenix, Arizona

We all heard the report by Dr. Hermona Soreq from Israel that was a very interesting piece of scientific research this morning. She happened to mention over lunch that the tricyclic anti-depressants depress acetylcholine, and that might be information you all want to take into account in deciding whether to use that drug.

Dr. Benjamin Natelson, Chair

Okay, I'm not sure. Again, if you have an injured cholinergic nervous system, but that's piling an if on an if, and in my experience, when caring for individuals with unexplained illness, the low-dose TCA's do help. The only other thing is that what we're trying to do is we're trying to be really practical. I think there was a comment made that picking a symptom is a little bit difficult when an individual has multi-symptom complaints. I hear you, but when I say to my patients, "If pain is one of your problems and I can take it down a notch, you're going to thank me, right?" So targeting a problem symptom is really appropriate in multi-symptom illness.

Dr. Ann Maddrey

If I could add one comment, and this is just based on experience. It's not a long experience, it's just experience that we have. We ask our veterans every week what their top three complaints are, and we've found that fatigue is the number one complaint from the vets. We have a list of the actual complaints from the veterans and how often they said them. So, you are certainly welcome to our experience, as little as it can be.

Dr. Benjamin Natelson, Chair

Thanks again. For the interest of time, if we can press on, then we can get a list and then, as a workshop with audience participation, we can shape and hown that list. So let's go on to longer-term, again, pharmaceuticals, including homeopathics, vitamins and minerals. Dan?

Dr. Dan Clauw

Sort of a statement followed by a recommendation; I think that we believe within the area of nutritional supplements, because they are not patented, the federal government is probably the only organization that's going to do randomized controlled trials. There's no such drug company that's going to fund a trial because there's so many different people that make them. So, a global recommendation would be that some type of committee or sub-committee be formed to look at the three or four nutritional supplements that might be most promising for treating this spectrum of illness and that those be studied in some type of randomized controlled trial.

Dr. Benjamin Natelson, Chair

So, that really is our input on the issue of vitamins and minerals. Now we had some endocrinology ideas.

Dr. Dan Clauw

Again, in the same line, that there is some evidence in fibromyalgia and chronic fatigue syndrome, that there are subclinical disturbances in adrenal function and thyroid function and that trials could be contemplated which would treat people with low doses of cortisol or low doses of thyroid replacement hormone to see if this might improve subsets of individuals.

Dr. Benjamin Natelson, Chair

So here, this is longer term because I'd think you would really want to find out what the effect -- when you give someone one of these medicines, you risk affecting their endocrine status. So here what we want to do is a real double-blind placebo controlled trial, where we had either a separate group who had either placebo or the active agent, or a cross-over design where the individual takes one and then washes out and then takes the other. Again, if we were doing a larger trial, we'd pick the first strategy. And here what we'd want to do is a minimum of a six to eight week trial, we'd want to use more specific measures of outcome than the ones, again, in the arenas that we discussed, and the low dose hydrocortisone in the 5 and 7 ½ mg range . . .

Dr. Dan Clauw

We should probably even say, very low-dose, so people know that we're talking about the 7.5mg, rather than the 25mg dose of hydrocortisone.

Dr. Benjamin Natelson, Chair

Right. If you realize that the body makes 25-30, the idea of the recent *Lancet* paper in civilians with chronic fatigue syndrome, is that this dose actually does raise the urinary excretion of cortisol, and then, also, similarly very low doses of thyroid, and we might be talking about the .05 mg range. Then, that would have to be backed up with the appropriate physiology, which would be assessment of the thyroid access and of the pituitary adrenal access, pre-post, backed up with appropriate physiology. So, these would be then the survey vehicles and the physiological probes. So, that's on the table then.

Panel Member

Just a question. Are we going to get printouts of this? Because I'm having a hard time reading it.

Dr. Benjamin Natelson, Chair

Yes, I'll get the typist, so I don't have to do this. I apologize. I'll try to print clearer.

Dr. Frederick Petty

If I could just make a suggestion regarding the nutritional supplements, I think fish oil, lecithin, vitamin E, and selenium are four things that I recommend to virtually all my patients, along with raw oatmeal. And it works. They come back and they say it helps. I also would suggest that we concur with, confer with Jerry Cote, National Institute of Mental Health, who knows more about natural treatments, including things like nutritional supplements, then probably everybody in this room, combined.

Dr. Benjamin Natelson, Chair

That takes care of that one. That gives me the sense that we are actually moving forward.

Dr. Wendy Wendler

Can I ask something? Are we leaving nutritional supplements, you're not using already existing nutritional studies, that have already been done? I'm a little confused by that funded by the U.S. Government. Is that all we're saying we're going to do?

Dr. Dan Clauw

No, again, we would try to decide what are the most promising nutritional supplements based on the existing data, or recommendations, but based on physiology.

Dr. Benjamin Natelson, Chair

If they are existing open label trials, that would point us, then we would do double-blind for the next step.

Dr. William Baumzweiger

Before we leave pharmaceuticals, what about the calcium channel blocker hypothesis?

Dr. Benjamin Natelson, Chair

I've heard your input. This is not a medicine I routinely use. I do use it personally in my practice for people who do have orthostatic hypotension, but I don't use it routinely for anything else, and you used it more generally . . .

Dr. William Baumzweiger

I've got to tell you, it's the only thing, and I've tried many combinations of medicines, which work, and it does actually improve patients' lymphocyte profiles. That was part of the paper that I handed out. There's a chart in the back, that it improves their immune system, if you give Nimotop and Gabitril and associated medicines, and I've kind of proved that. And, actually, frankly, if you don't put it on there, I'm going to feel this is a continuing stonewalling of my work, which many of the veterans are very upset about.

Dr. Benjamin Natelson, Chair

Listen, I'm happy to put it in. You have to understand, Dr. Baumzweiger, the logic of what I think we have tried to do, has been to take medicines that have been known to do, known mechanisms, and have been shown by more than one person, to be efficacious. The pain regimen is relatively unarguable.

Dr. William Baumzweiger

Effexor toxicity is completely known.

Dr. Stuart Brooks

I think it's an interesting observation. But I think, our group, for example, went through there,

there's a lot of outcomes, a lot of things that treatment would be addressed to. One might be fatigue. I think the calcium channel blockers might be more for this autonomic imbalance, so that if one of the outcomes that they're looking at, is a measure of autonomic imbalance, the resting or standing pulse rate, like you did, then this might be appropriate to use that. But if the study deals with, let's say, depression, or if it deals with true quality of life, it may not be the drug that they'd want to use.

Dr. William Baumzweiger

Depression, autonomic signs, cognitive attentional problems, fatigue are all brain stem limbic system signs. You're all talking sub-cortical stuff and that's what I'm talking about too.

Dr. Benjamin Natelson, Chair

Okay, let's do this. Here's my compromise. I think what we'll do in our sub-group is we will come up with a treatment protocol for the symptoms of orthostatic intolerance, as defined by either heart rate increase or blood pressure decrease with posture. And we'll hash that out, you and us, after this session, and we'll get a trial down on paper. Fine. That way, we'll get everyone's ideas.

Dr. Stuart Brooks

Did you use beta blockers or anything, too? Have you tried other things?

Dr. William Baumzweiger

I actually feel that because there is fatigue and slowing, beta blockers would be contradictory. Again, you're fooling around with the acetylcholinergic nervous system. I don't like doing that. I'm very conservative.

Dr. Benjamin Natelson, Chair

Well, I think that we can certainly come up with, again, this is neurologists' sort of bread and butter, a treatment protocol for orthostatic intolerance, and we ought to be able to come up with a plan.

LTC Charles Engel

The one request that I would have, Bill, is if there is existing data, looking at the use of calcium channel blockers, maybe it could be made generally available to us.

Dr. William Baumzweiger

I'll send you a reprint of my article which was published last year on calcium channel blockers in the treatment of orthostatic tachycardia. And we did also a factor analysis of 27 symptoms including depression, anxiety, headaches, and calcium channel blockers have a modest improvement in symptom clusters in 17 out of 27 Gulf War symptoms. I'll send you that article.

Dr. Dan Clauw

I'm not saying that to challenge, but I'm really saying it more from the general standpoint that I think we have to use evidence to decide which are the best medications.

Dr. William Baumzweiger

Well, this came from a peer-reviewed journal, so I think it's evidence.

Dr. Dan Clauw

I'm not doubting that.

Dr. Frederick Petty

My concern is as follows. I have now been working for your United States Government for 19 years, 3 months, one day, and about 14 ½ hours. And the minute that this report is signed off by your committee, it's going to become codified in the sclerotic policy and the door will be slammed shut on any innovative new idea. And you need to put a clause in there to keep that from happening. For example, we've got some pilot data that I have not yet finished analyzing, that strongly implicates the GABA system in Persian Gulf War veterans with PTSD. Now, God knows, there are not many of them, but, if this pans out, we would want to propose a treatment trial focused on GABA agonists.

Dr. Benjamin Natelson, Chair

Please understand, I don't think that you're right, Dr. Petty. If you have data that point to a defect in a neurotransmitter, a neuromodulator, then you can do what all of us have done, which is put it into an RO1 format and propose the trial. And that will go through peer review and I think . . .

Dr. Frederick Petty

That doesn't get the peer review. That gets ignored, because I did that eight months ago.

Dr. Benjamin Natelson, Chair

Well, listen. The name of the game in academic research, if you'll excuse me, is rejection. And you're looking at someone who has to write eight grants to get one. That's the name of our game. So, zero for one, you're okay. So let's push on then. Group 2, Non-Pharmacologic.

Dr. Michael Sharpe

Clearly, there are issues of . . . this is research. We're going to talk about things that could be done to help people, but clearly there are issues of how the evaluations are done. And whilst we obviously would argue that a randomized trial is going to be the gold standard way of evaluating these, for some of the immediate ones, there may be some more difficulties in that and some simpler means of evaluation may be necessary.

The second point we wanted to make, is for the early treatments, that they should be based rather than on the pejorative cause, because we don't know what the pejorative cause is, on a measurement of people's actual needs and we'd employ a needs assessment approach to work out what people's needs are. And we can talk about what domains they may be in, but for example, there may be certain needs to be able to communicate with people who have similar problems, there may be mobility needs, there may be needs about getting sleep, but the immediate, given we know that these are people with heterogenous needs, the earliest interventions were based on needs assessment.

The actual interventions, we thought that the immediate ones could best be borrowed from similar overlapping conditions and would really be based on symptom-focused interventions. Those have pretty wide-spread acceptance. So, for example, strategies for coping with pain, strategies for improving sleep quality, strategies for dealing with memory difficulties. There's a well-established body of literature in practice for these problems in different populations, head injury populations, chronic pain populations, chronic fatigue, and so on. How these would be levered, obviously, there are options here.

One thing we thought, is that people could be given useful self-help material, based on the needs assessment. It also might be possible to give their physicians similar material. That would be the first step, if you like, of the early intervention. There could be further steps. One could be brief help by a physician or by a nurse in implementing some of those strategies, then, as the next stage, there could be using the intensive multi-disciplinary rehabilitation programs that are widely used in disabling conditions. These could either be evaluated separately or they could perhaps be evaluated as part of a step care model. That is, people only go on to the next step if they don't benefit adequately from the first step. So, it could be evaluated as a whole management protocol.

That's really the essence of our -- now, we're not really specifying in detail what those specific

interventions could be, but that would be the strategy that we would suggest.

Dr. Benjamin Natelson, Chair

This is all short-term, right? Or is this everything?

Dr. Michael Sharpe

We're not quite sure where the boundary for short-term and long-term lies, but that's kind of stuff that we could implement. We don't need any new ideas, really to implement this. It's just really a matter of implementation.

Dr. Benjamin Natelson, Chair

Can you for me, taking the Chairman's role, come up with new ideas where you need randomized control trials for the long-term? Because I'd think we'd like to do both.

Dr. Anne Solomon

In the needs assessment, we want to be certain that there is a whole space, if you will, left, for people to give us their new ideas. In other words, the needs assessment is not only to answer the questions that are there, even though it has a strong communication component in it, which is a new idea, if you will, we want to establish communication with these people, and to help them to establish communication with their doctors and with one another through this instrument. But, that would be one area where there are new ideas which are being solicited from veterans, okay, and then we do have a fourth component which also has a place for new ideas.

Dr. Michael Sharpe

Yes, we haven't finished. I stopped at the end of the short-term.

Dr. Benjamin Natelson, Chair

Okay, let's ask you to stop there then.

Mr. Anthony Hardie
Constituent Liaison, Veterans' Affairs
Office of US Representative Tammy Baldwin
2nd District of Wisconsin
Madison, Wisconsin

I'm a bit concerned when I hear that you would not be able to go to the next step unless the first step is not necessarily effective. It doesn't sound like that gives any local physicians any kind of freedom. It sounds like what we've got at the VA now, which is not working.

LTC Charles Engel

I'm not sure -- could you spell out in a little bit more detail what your concern is?

Mr. Anthony Hardie

Sure. You mentioned that the plan would not allow you to go from one stage to the next stage unless the previous stage had proved to be ineffective. Are you following me?

LTC Charles Engel

I think one of the things that would be the focus of the evaluation would be the various steps and I think overlying this is the fact that the patients are going to be seeing their physicians for this and other things and it may be that the physician decides to refer them, based on their needs at the present time, to a more intense step. I don't think we want to buy in so rigidly that one has to buy into A and strike out before getting to B, in which case it may be a long time before they reach some of the more intensive therapies. Especially if we know at baseline that they have a fairly chronic condition, and in many ways they've already attempted to use a lot of the less intensive approaches.

Mr. Anthony Hardie

I like the idea, and I think the multi-tiered approach seems to make an awful lot of sense, but I just get concerned when I hear about it being very restrictive, that it doesn't give local physicians a lot of . . .

Dr. Michael Sharpe

I think the steps were just put in there as something to think about. I think probably these things would be evaluated independently, but based on people's needs rather than just giving everybody the same thing.

Mr. Kirt Love

One of the things that I have personally run through, in my own VA appeal, now on number four, many times veterans don't know what information to offer or what things to offer, especially with neurological exposures. They don't know to request a neurologist. They don't know to request

that part of the evaluation, and therefore, these people tend to fall through these loops. I deal with a lot of individuals that exhibit neuropathy and other things of that nature, and if you give them Class I, they'll never make it to Class II. And I think that maybe we should put at least a little bit more restrictive guidelines, give them a little bit more benefit of the doubt, especially with neurological. And that's one of the big ones that I've had specific problems with. I never knew until the third evaluation, when I finally, accidentally requested a Neurologist, I sat down with him and he said, "You can't fake not having reflexes. You can't fake this kind of lack of sensitivity to pain." You can't fake the disorientation and other problems that I have. And I never knew about that, and many of the people that I talk with, have no idea. So, maybe we should try to go a little bit further, at least with some of these.

LTC Charles Engel

Point well taken. Another point to make about this approach, is it goes beyond what's already being done, or not done, in most cases, in the sense that, the idea of the needs assessment is population-based. In other words, whether you have identified yourself as someone who is ill, this sort of needs assessment would go to you and everyone would have the opportunity to identify needs that they have. And based on what needs come forward, we would be designing interventions to match them.

Mr. Kirt Love

But at the VA facilities that I've been dealing with, there's sort of an adversarial approach by many of the doctors. And, when there's an adversarial approach, it's annotated that you have a psychiatric disorder, so rather than a complete follow-through, they're busy trying to send you down to Psych and give you Prozac.

Dr. Benjamin Natelson, Chair

Again, I hear you. That's what we're all about. This is not same ol', same ol'. This is a trial. We're trying to design a trial for a symptomatic Gulf vet, where he would be on a different kind of escalator, an escalator that would move him toward health. This way, where you are going, because it's all laid out and protocolized, that won't happen. All you have to do is be enrolled in the trial.

Mr. Kirt Love

Oh, I understand that, and it wasn't my intent here. I'm just basically expressing what has happened to me, personally, and interjecting that as a personal experience, not meant to contradict.

Dr. Benjamin Natelson, Chair

Oh, I see. Well, hopefully this would work for you and it would work for you in two senses. One, you won't get that because the researcher needs you desperately. He doesn't want to say go that-a-way because then, he's never going to get the answer. I mean, the problem we have in doing our research, is always the problem of getting the willing volunteers.

Mr. Kirt Love

Well, another point, I've already had my second or third CCEP and so on, and so on. Still have not had the SPECT, still not DU, and there's several tests that still have not been done that I would prefer done. Others I've paid for, like the MRI, out of my own pocket. So, I mean, it's still an ongoing process.

LTC Charles Engel

One comment I want to make about this sort of approach, is that, in the ultimate stepped care approach to this that one source of frustration on the part of many physicians, and this occurs with anyone with lots of physical symptoms of the sort that Gulf War veterans frequently describe, is that they view their encounter in the form of a 10- or 15-minute visit and physicians, quite frankly, get overwhelmed so what we're trying to construct is a mechanism, a structure of care that would, to a certain extent, alleviate the healthcare provider, the physician, of having to respond to everything – that there would be a delegation of care within the context of that so that other appropriate professionals could also assist at the various levels of that care.

Mr. Kirt Love

One point I just want to introduce on that, a lot of times we're so sick and so frustrated, that we tend to be overly aggressive and that tends to kind of trip ourselves up when we talk to these doctors. A lot of times, by the time you finally get in the room, you're so angry, that you tend to, a lot of people, like myself, over-react. And that tends to trip things up, as well. Hopefully, the new teams will be ready to deal with individuals who may be overtly hostile, although, not intentionally. Hopefully we can address that point and make them ready to deal with these issues, rather than make them a psychiatric case – to hopefully see them as very frustrated, and hopefully address it a little differently.

Dr. Benjamin Natelson, Chair

That's really a good point and I personally thank you for that. That's really a good point.

Ms. Wendy Wendler

One of the things we do is try to have somebody accompany the veterans. I don't want to say they're inarticulate because they're dumb, they literally are having such memory loss, they can't give you all, or the doctors, the clues they need. I just came from a VA meeting with a woman the other day, with a neurologist, and it was just hopeless. She was literally showing him the symptoms by not being able to answer his questions. The resident with him came out afterwards and said it would be great if you came with her again, and I thought, "Yeah, but you know, there's no gasoline money and there's no funding."

So, when the advocates seem to be butting in, we're really just trying to be facilitators. I literally remember her medical history for the last five years better than she does. There's also some gender components here. A lot of times, they're trained not to tell you things. Besides the Top Secret clearance part of military training they're trained to "suck 'em up, Marine." As one mother told me, she said, "I can't even get him tell the doctor when he's in agony. He really won't tell him. I have to tattle on him to the doctor." So, I think you're all hitting the idea that there are some sociological components to eliciting information, and I can see the frustration of the researchers as well and that's where the advocates would really like to be an agent.

Dr. Benjamin Natelson, Chair

Absolutely, and there's no question that those social and sociological issues are researchable also. The VA wants its customer base. The VA wants the veteran to come to the VA center and not to wherever, not to the University hospital.

Ms. Wendy Wendler

Well, we're trying to work on a patient log that I used when I was very ill and detoxing. And really, I wouldn't remember one day to the next, but when I looked over a five-day period, and the social security judge took my little handwritten log for one month, when I wanted my benefits, he said, "That was one of the most important pieces of evidence you brought. I'll accept that." And it was just amazing. We just did -- my hair's falling out -- my eyes -- whatever, we just went down and it would apply to – if you kept a patient log, different researchers could find their piece of data in there that they need.

Dr. Don Salisbury

I just wanted to stand up here and speak in support of this proposal. These are things that we need. Working with veterans on a daily basis who served in the Gulf and who are sick, these are things that are very obvious to us. They need the patient advocates, we would hope to, in that in the system, such as Sonny Montgomery proposed in a teleconference, videoconference that he did a year and one-half ago with the Birmingham VA folks, talking about the nurse case manager

concept, how it has worked so well in Birmingham, and how it's really improved care. Because at that time you can really help them identify what they're needs are, and help them get those needs and work through that system, which sometimes seems uncaring, sometimes seems like they have cold hearts and tin ears, which some people have said that we have. I think it's more of a bureaucracy and this would help them get through that bureaucratic system, so I think this is very, very – I think this is obviously going to show a beneficial outcome for the veterans. It's sort of a slam dunk. It also reminds me of the Walter Reed Program, where the health center there is working with the veterans in many of these areas. Some of the veterans, or the active duty people, who are now veterans, who have gone through the program and it's a multi-disciplinary approach that really needs to be ingrained in the system. I just don't know though, if it's going to be redundant what the VA's doing in their demonstration trials. They have a number . . . (interrupted).

LTC Charles Engel

Not the treatment trials, the demonstration trial, which the VA started last summer. They had eight sites around the country, which they asked the Gulf War programs to propose a demonstration study. I know Birmingham was one of those, I'm not sure what the other seven were. They didn't get much in the way of response. When Fran Murphy and Susan requested people to volunteer for this, I don't know if there is not a VA of those seven, that are actually doing it, if they followed through. I haven't heard anything more from Fran or Susan about whether or not those are up and running. I know the Birmingham people are doing their program. But, is it anything like this and is it already being done?

Dr. Don Salisbury

It is similar in certain elements. It's probably more similar to the program we run, which I think borrows some elements from this, or contributes some elements to this, but it's more along the line of step 3. What doesn't exist right now as I see it, and the thing I would add is, it only exists in half a dozen medical centers around the country. And in DoD, our program, is the only one. So, what this could lend itself to, is a very wide population-based strategy of care that has both pre-care elements, a needs assessment, before people necessarily even visit care, primary care elements, so bringing maybe less intensive strategies to a less ill population generally, and for those with sufficient needs, this sort of collaborative primary care, and then ultimately, sort of a more multi-disciplinary model like what the demonstration projects have. The other thing about the demonstration projects is that they've been conceptualized as clinical pilot projects. They haven't been conceptualized as something that is going to give us clear research results that are going to be easily interpretable. So, it's an attempt to implement programs in ways that allow data to be generated around it.

LTC Charles Engel

I just want to ask one other thing. Is this going to, because this is non-pharmacological group, is this also going to look at those other unconventional programs such as . . .

Dr. Benjamin Natelson, Chair

Just let the veterans come forth, please. I'm not going to let that General yell at me again, darn it. I'm not as dumb as I look.

Dan E. Jones, PhD
Director, Post-Traumatic Stress Recovery
Oklahoma City VA Medical Center

I'm also a veteran, so I can speak to that. From the perspective of a clinical psychologist, first, in principle, I really agree with the proposal we have here. In practice, I have a couple of things that I think we need to be reminded of, or be aware of.

First, if someone is willing to fill out a needs assessment, if someone asks to participate in a randomized trial, I think they're doing that with the expectation of getting some help from a professional. Immediately referring them for self-help gives them the idea that maybe they've done the wrong thing sometimes or maybe they should have been able to do it on their own, and now you're saying that you've got to go back and start from square one. Going from step one to step two can also be problematic, in saying that you've tried self-help and you were not successful, you were a failure, you were no good at what you should have been doing, so now you've got to go get professional help. I think we need to be aware that there's some resistance to that, there's already distrust or mistrust, especially among the veteran population or those providing services. So, if we can let them know that it's not because they're a failure, it's not because we expect success in the first place, that we are suggesting these things, but maybe there are some things that we can help with or that could do on their own, that they could be aware of before they even start.

Dr. Benjamin Natelson, Chair

That's a great point. If a veteran is seeing a professional, he's already at step two, sort of. Right? I guess you can say to the veteran, here read this. How do you deal with this?

Dr. Michael Sharpe

I don't know exactly what happens with folks now, because I'm not even from this country, but I would be surprised if many of the people who are already seeing people are getting proper in-depth needs assessments, and we can see that these wouldn't just be something in the mail, these would be done by a nurse or an occupational therapist. These could be quite extensive

assessments. So, I don't think the fact that they're already seeing someone would mean that's already done. And furthermore, I think adding tailored self-help information to it, again I would be surprised, unless this country is even more advanced than I think it is, that these people would all be getting detailed information on how to manage their own symptoms from their existing docs. That would be very unusual. And, I think the idea that if you fail in self-help, you're a failure, I think it's right to guard against that, but if the whole thing is sold on how we best meet your needs, and say, we'll actually, that didn't meet your needs, you need something extra, I think it can be sold to avoid the sense of failure.

Deborah Moodie, RNP
Secretary
New England Persian Veterans, Inc.
Craftsbury, Vermont

I'm an RN, and just to go along with what you're saying, I'm thinking, where's the nurse in all of this? I know my job, as a nurse, when I first see a patient, the first thing I do is my head-to-toe assessment. And if you've got a good nurse doing their job, to me, make sure you're well staffed when you're doing this and have the Nurse to the head to toe. Maybe something can be drawn up ahead of time. But if they can't do their job from their schooling, but, do the good head-to-toe assessment, and if there is need for the nurse to be in there during the exam, that would come up on the assessment. So maybe you need to make sure that you have not only the Physician doing this, but a nurse right there hand-to-hand, doing these studies.

Dr. Michael Sharpe

We didn't actually concede that this would probably be done, or at least not all of this would be done by a physician, because a) they may not be very good at it; and b) they would be unlikely to spend the requisite time. In the UK model, we're using this kind of thing with chronic fatigue syndrome, in the UK, with nurses doing it. But, whether the nurse in this country is the obvious person, or whether it's an occupational therapist, I'll let my colleagues say.

Dr. Anne Solomon

We thought the occupational therapy situation, which, actually, I've been quite impressed with a number of the occupational therapists in the VA system, and others, they really are pretty good at this. So, that's another possibility. It could depend on hospital to hospital, but they really have this sense of the problems people are having every day with accomplishing certain tasks and basic things, and what sort of steps need to be taken one at a time, to help them overcome some of those problems.

Mr. Anthony Hardie

Right now, one of the flaws that we have that the veterans are seeing is that there's very little outreach by the VAs and that you really have to just show up. I'm from Wisconsin, and in Wisconsin, we have people who live in the northwoods, five hours from the nearest VA facility. It seems like the self-help, and the point that was made earlier, if you're coming to see a physician, you're already at step two, why don't we push for, if you put in a recommendation for the self-help bit, that there's some sort of a recommendation for a guide or self-help booklet that's sent out to all Gulf War veterans. Of course it's expensive, but this is how we're going to get outreach and credibility. Perhaps they could check off if they want brochures or further self-help, that would be step one, A. And then leading into step two.

LTC Charles Engel

In fact, what we would propose is a step further than that in which one issue to study would be to take a group and send them that sort of a book, and then, take another group and design literature that specifically addresses their needs as they are assessed in an instrument like this, and send them that, and look to see if there is added benefit to self-help literature that specifically targets the needs of the individual, versus some generic book that in the end, ends up turning us off, that this is the VAs feeble way of telling us that they care. Do you know what I'm saying?

Mr. Anthony Hardie

Yeah, and again, the sociological aspects are incredibly important. When I first left the military, we used a dumbing-down of vocabulary to make things as concise as possible, and when somebody's shooting at you, you want to say things as quickly as possible, you don't needs lots of extraneous vocabulary to describe it. I tell my wife I don't know what's wrong with me. I'm confused. And her response is, "Well honey, we're all confused." So we need to think about how to address veterans, especially that are just re-emerging from the military, so that they can actually communicate what it is that they're experiencing.

Dr. Vinh Cam

If I may, I would like to add something. It's not a research issue, it's more of an organizational issue, but I think it would be critical. If it's possible, I would encourage researchers to utilize the talents among the Gulf War veterans. Some of them may still be in the government, some of them may be out, some may be in the transition, but utilize the nurses, health care providers, because they have a lot to give. Not only the expertise, but the professional experience and they could help the researchers put things into context, so that when someone says, "I'm confused," it could be because of so and so. So it really is a human resource issue and I'm a civilian. I don't know how things work within the Pentagon or the VA, but I urge everyone to keep that in mind. I think it would help tremendously.

Dr. Benjamin Natelson, Chair

That's helpful. When the VA hires, it always wants to hire a vet, but when it's downsizing, of course, that's the opposite, unfortunately. Number Four.

Dr. Michael Sharpe

What we have focused on is the things that we could do, like tomorrow, if we had enough money and energy to do it. Part Four, we wanted to make it very clear that because we based Part One on things that were off the peg, things that were established, we didn't want to make a statement we're excluding new ideas. And therefore, the longer term, which are ideas that may need a bit of working out and a bit of thought, would be first, if necessary, simple evaluations, non-randomized evaluations, and then, if they pass muster randomized trials, of more novel interventions. These would include perhaps, some of the alternative complimentary medicine treatments that I think our group was tasked with, but I think also, the specific psychological treatments that are based on more examination of the issues. For example, there's a generic cognitive behavioral program that is going to be done, so we've ticked that off, because that's already being done, but it may be that more experience with that would generate more acceptable, more helpful treatment, and we wouldn't want to feel that was necessarily closed as an option.

Dr. Benjamin Natelson, Chair

That makes sense. If, when you do a CBT trial, you find that the protocol needs to be tweaked and can be better, that's obvious. Great. If there's no problem with that, we'll move on to the next group, which is Macro.

Dr. Stuart Brooks

Our group had long discussions to put out what conceptually what all these programs depend on, and using this as a model. Let's say you have something like a back injury, where you're hoping that someone is going to get recovery. In that recovery from the back injury, you look at it as structure, process, and then outcome. In the structure, you have a patient, a family, a doctor, an advocate, the VA, the DoD. In the process, there is the culture; what the person has repressed, the education of the physician; whether the person can diagnose a back injury, whether they even believe the patient, their attitude, the training of the lab technician, the X-ray. So, when you start talking about how long the person's been off from work before they're evaluated, and when you talk about recovery with medication, you're really fooling yourself if you don't look at these other important factors.

Consequently, just medication may not be the only factor. So, you need a milieu where the therapy is going to be working the optimum. What I have here is all the various things that would

be in the structure, the process and the outcome. For example, structure: you have a case manager, the scheduler, the laboratory, the social worker, the family, the advocate support group, the media, the attorney, the Department of Defense, the VA, Congress. Here, the education, the training, the protocol with case definition, the attitude, the networks, family input, compensation, diagnostic criteria, testing done, selection, when it's done. Other: lifestyle, other diseases, other exposures. And when you talk about Outcomes: is it biological, physiological, quality of life, less medications, more sleep, being able to function better, less depression, psychological cognitive.

The point is, it's a complicated thing. In order to look at that, we think that what's needed is a research treatment multi-interdisciplinary model to establish the central processing unit that can deal with some of these issues that were brought up. First of all, short-term would be to establish this center, which would enhance communication, enhance education to both the physicians, nurses, administrators, vets, patients, and others, and provide some outreach between these various groups. As part of that, a variety of different kinds of research. This would be results, eligibility, recruitment, hotline information, quality surveys. These are just some of the things that could be done.

The long-term would then be to conduct a variety of research that deals with how the service is delivered, does, for example, the self-help books really influence outcome? For example, somebody comes in, they have a book on self-help, or something that explains the disease, and then they go in to see the doctor, the program. Does that really influence outcome? Is it like a placebo? And I think with diseases, with processes where there's multi-organ problems, and cognitive difficulty, these other stressors, these other influences, play a big role in successful outcomes. So, what we really want to do, is have a successful outcome, not put too much stress, not put all these other things that produce anger. What this multi-disciplinary group will be which enhances communication and education, will centralize the information, will allow communication to the various support groups and interact with the advocate groups, and then, work with the researcher in obtaining the information. I think that will deal with this process that will enhance some of these other things that we've talked about, and ensure that the outcomes are going to be the outcomes more likely for the treatment than from influences of not being able to get anything, frustrated.

For example, if there is a study trying to divide eligibility and a central place to recruit patients for a study that might be, for example, in Colorado, but being able to recruit from all over the Country, and giving the criteria, so people could then get the criteria, maybe get the first step going through this central group. Then you could have a population that may be selected on certain criteria, based on this initial evaluation. So, that's what this Macro is. To deal with all of these other things that have been brought up repeatedly to deal with making communication, education and outreach, putting it in a central point and this could also be a source of newsletters. One of the models of the post traumatic stress disorder center and what they do -- Why don't you just go ahead?

Dr. Nancy Fiedler

Dan Jones brought this to my attention and I think it's a very nice model. It's the National Center for Post-Traumatic Stress Disorder, and in fact, I get their newsletters. I don't know, in fact, what-all they do, but that's part of what this might be modeled after because it takes a feature article in what's going on in the research and clinical fields, in terms of treatments and gives abstracts for studies in terms of the outcomes of various studies. So, what we're proposing is maybe somewhat similar.

Dr. Stuart Brooks

More expanded. Some of the functions that it sounds like you're doing to communicate both ways and deal with some of these other issues.

Dr. Nancy Fiedler

Right. Because I think it's very hard for some of the veterans, certainly every veteran who participates in a research study should get that feedback from their participation. But, it's very hard to get a big picture of all the research going on and what the outcomes are, and this would be a vehicle for doing that. And in terms of, we're supposed to write a research question, these kinds of outreach studies can be put into research questions and can be put out for RFPs to look at the effect of this on attitudes. For example, one of the models proposed here was to educate healthcare providers about the needs of Gulf War veterans. Then you could evaluate that.

Dr. Stuart Brooks

One of the things that we said was an Audit. For example, is there everything that's adequate in that organization? Do they have enough staff, enough laboratory facilities, do they have the things that are necessary to conduct the study at that particular institution?

Dr. Benjamin Natelson, Chair

From the researcher's point of view, this approach is wonderful, because again, what the researcher has to do is recruit, say forty vets that fall in a specific box. If the veterans are here, then that's a place you can go to for the recruiting. You don't have to look in your little area.

Ms. Deborah Moodie

I think your idea is really great, but right now, the sick veterans are a really tight-knit group, and they're really doing this now to protect themselves and each other. This would be great, but it should be veterans.

Dr. Stuart Brooks

That would be part of it.

Dr. Deborah Moodie

I think you ought to have them where they feel that the veterans are controlling this and you're going to get a better response.

Dr. Stuart Brooks

The short-term would be how you establish it. How you establish it is open. But I think it has to be multi-disciplinary. Everybody has to be part of it. It can't just be veterans, because just by our communicating, for example, in my case, I understand better what the issues are. You're probably the same way. These are the problems with research. This is an epidemiologic study, this is a problem. So, that two-way communication can then be something, where each of us learns. So, having just veterans on this group, it's really an advisory group, but it's also an outreach communications group, and when talking about outreach, you're talking about outreaching everybody. So you have to have everybody's input.

Audience Member

But there is a high level of suspicion, Sir.

Dr. Dan Jones

If I may, let me draw a few parallels between these two things. Number one, I do not want to say every Persian Gulf veteran has PTSD. As a matter of fact, just the opposite. I thinks it's a very small percentage that has that. And I note they don't want to be accused of having PTSD, I'm not trying to do that. But there are some similarities in the process here. I got out of the military in 1970. I was in Vietnam in '68, '69. There were a number of people who were veterans having a compilation of symptoms that they were not getting diagnosed properly for – mis-diagnosed many times. A diagnosis did not exist for their disorder. PTSD did not exist until 1980. But there were enough veterans that started to speak up, appear at the VA saying I have these sets of problems, that they finally developed treatment resources for them. Finally developed was the National Center for PTSD. This organization facilitates the resource development, the research, the treatment resources, the funding resources, it speaks with a national voice to the Congress, the Department of Veterans' Affairs, it has a number of different researchers across the Country from not only the VA, but also other outside sources, so it's not uni-dimensional, and I think it addresses almost every single one of the problems that we've been discussing.

Dr. Nancy Fiedler

I agree, and I thinks that's why we grabbed a hold of it. It wasn't, it's just the analogy. But what I wanted to say about one of the things you brought up earlier is that one of the things that we've developed in our institute is that we deal with occupational and environmental health problems and I think your point is very well taken. One of the issues that has come up is that very often where communities have contamination problems, we go out to the community, sort of as the experts, and become mis-trusted by the community and the people don't want to cooperate in our research studies and our exposure studies and the model that has come about is an outreach model like what we've been talking about here. We get community members involved and we call them the stakeholders. The community is involved in informing the researchers about what they're concerns are, and that gets built into the research process. There are models out there to use to help with this problem.

Mr. Anthony Hardie

The position of the National Gulf War Resource Center has, for some time, been that veterans do participate in the treatment and the research, and so on, and this looks like it's definitely in keeping with what we've been asking. The second point I'd like to make, on more of a personal point, is the VA system. It's very important that we keep the Persian Gulf War coordinators at the VA hospitals involved, and right now, they're often underfunded positions, or they're part time positions and so on. I would like to see that they are mandatorily involved from the beginning and that they're required to, whether it be they're required to watch and certify a video of the proceedings or whether it be to actually attend conferences and so on, but that these Gulf War coordinators are mandatorily involved with this process to ensure that each VA hospital has at least one person who understands the importance of the research. I'm going to give a brief example of what happens when that doesn't happen. I've been requesting to go to the multiple chemical sensitivity study in Houston, Texas for quite some time. I've been told that because I have a diagnosed condition of chronic sinusitis, which I believe is actually a symptom of whatever the problem is, that I am no longer eligible to do so. This has been checked off as okay by the Gulf War coordinator because she doesn't understand the significance of the research. This is why it makes a lot of sense to have them mandatorily involved in the entire process from start to finish. Thank you.

LTC Charles Engel

I agree. I would also say this discussion is extremely timely from the standpoint that currently the VA has contracted with the Institute of Medicine to study the formation of what they're currently calling the Center for Post-War illness. At the same time, DoD is forming a similar effort and the idea is to ultimately collaborate with the VA and our effort to date has been called the Centers for Deployment Health, but I think the ultimate idea is to eventually put our ideas together in a

collaborative way that would function something like what we're seeing here.

Ms. Wendy Wendler

We would really like to applaud that this particular idea is really gelling. The VA already has existing programs, and PTSD is such a bell-ringer, they have such programs for women, American Indians, spinal injuries and maybe that's some of the examples and models particularly the spinal injury center in Dallas and the women's programs in every VA mostly, and the Persian Gulf Coordinators are in a really difficult position. When the Showtime movie came out, the Persian Gulf coordinator in Dallas said to me, when I invited him out to attend, he was busy, he had a conflict in scheduling and he's also the Agent Orange registry person, he said, "You know, this is really sort of like Agent Orange. There really is no such illness as Persian Gulf illness," and he is the Persian Gulf coordinator. So, you know, maybe this is a place to blend in some of the local advocates, I'd say activates, but people who actually do something, maybe they should be either a volunteer Red Cross worker; the Red Cross is chartered by Congress to do a lot of what you all need to get done. Mrs. Dole, when she was President of the Red Cross during the Persian Gulf War, gave back $13 million and said they were supposed to help veterans when they returned from the war, and no veterans needed it. Nobody asked them for it, and she even gave it back to the Pentagon. So, I mean, there are these wonderful precedents, we just didn't know that we needed, in a timely manner.

Also, there is a precedent in the state of Oklahoma, and these state programs are really key at the state level, but in Oklahoma City, Mrs. Whitcomb started a working group, and HBA would have one, theoretically, that the Persian Gulf coordinator representative of the director of the hospital, and they met once a month for almost a couple of years. It was amazing in two or three minutes having a cup of tea together on the first Thursday afternoon of every month, or whatever, they would just say, "Oh, I didn't know that," and "You told me that," I mean, she was literally bringing information to tell people at the VA what somebody at another VA was doing through our networking system.

Also, for about four years we've been talking about something called a medical boot camp. I'd certainly be happy to use any more military terms more suitable. But it's just particularly interesting to think that it's very difficult to do some of this outpatient. They need to be sort of like, "Calgon take me away." You know, put them in a setting where they can be rehabilitated in a very effective financial arrangement. Also, I would remind you that many of these people are being carried on IRR, individual ready reserves. They hid thousands of Gulf War vets who were ill that didn't show up on the active duty roles as sick, but they didn't get dumped back in the civilian community because the VA couldn't handle it. That's my opinion of how it worked. But with the stoke of a pen, the President can recall literally all 200,000 reserves, then he'd have to ask Congress, and they'd be getting some monies, they would be supported, we could literally just fit them back in the system. I worked the peak casualty period of the Vietnam War, and we did

not send sons home to their mothers with bloody legs and stumps in baskets. This thing is ridiculous. We kept people in traction for maybe 13 months at Fitzsimmons Army Hospital because they were soldiers and they were injured and they were casualties and it was honorable, and they were getting paid and they were wounded, and their orders were to get well and get back in shape, and they did it. And I think we just dumped them back on the civilian community and we just dumped them on a VA system that was utterly unprepared with this, and so it's really not their fault. We just need to rethink these.

There's one more point I'd like to make about some of the socializing of this. In the Agent Orange case, they were telling us this hostility and anger was, of course, very valid, and not just psychotic, but that once, in family violence, for instance, when children are abused, it's one thing to be abused by a stranger. You know, you can have an enemy or you can have a villain, but when you're abused by someone you love or that you thought loved you, that it literally changes, and I know some psychologist will know of some behavior disorder this is called, and I think if we turn these people back into soldiers again -- If Jason had lost an arm, he might be handling what's happened to him so differently. I understand there's some psychological phenomenon in counseling that restores family violence and problems, and maybe this is just the key to putting them back in the position they belong in.

Dr. William Meggs

This group is based on the testimony of veterans here at this meeting who reported that they went to certain private clinics, and with a great sense of enthusiasm and strength, feel that they were helped by the routines there and there were a couple of modalities that we've used. One was the detoxification clinic that Dr. Root has talked about, and the other one is a clinic that uses a combination of detoxification with some elimination of foods and chemical exposures and so forth. And so, using Congressman Sanders' charge that we should quickly look at some of these therapies, and treat some veterans and see if they work, and see what happens and then see if we should broaden this and offer it to other veterans.

On the short term, we propose four pilot studies, and these studies should be controlled and blinded. And we think with these studies, patient selection is very, very important. It should be a homogeneous population of patients, it should be patients who meet certain criteria. It would be the poly-symptomatic groups of patients for whom all medical causes like leishmaniasis, DU toxicity and so forth, have been eliminated, because we don't want to be looking at private detoxified patients suffering from heavy metal poisoning or some other thing. And there should be pre- and post-treatment assessments and this should be blinded and controlled.

Now, how do you blind control it? And here's how you do it. You select two age and sex matched, education matched, groups of veterans and you send one to the treatment and the other doesn't get the treatment and you have assessment teams of physicians, neuropsychologists,

whatever you decide, to do pre-treatment assessments, and do post-treatment assessments. And the rule is, these people do not know who went for the treatment. That's the best we can do. We can't blind the sauna bath, we can't blind the bicycle machine or get rid of your gas stove. And then the assessments would be, use self-assessment instrument symptom scores, quality of life instruments, neuro-psychiatric assessment is important, and one symptom at least anecdotally, seems to be greatly helped by this is the people who have cerebral problems with cognitive dysfunction and short-term memory. In my own practice, I don't do this kind of work, and I don't refer people to this kind of treatment, but since I saw neurotoxicity patients who have, on their own, gone out and taken these treatments, come back to me and said, "This is the one thing that helps me. I think I'm much better." So, neuropsychiatric assessments might be important.

And we think it's also important from the detoxification part, to monitor levels of chemicals. We've heard descriptions of yellow gunk coming out in sweat and black materials coming out in the feet. Well, let's do GC mass SPECT on this to see what's in it. Let's do other things like, serum. We've heard that the CDC measures volatile organic chemicals in the serum, maybe urine elimination, collect fat, it may be appropriate for some chemicals, and send them off. Now, this is supposed to be short-term, and how are you going to undertake this in the short-term? The only thing we came up with is you have clinics out there doing this, so you should send a group of veterans to these clinics, and have your two control groups. You'll have the cooperation of the people that do these things, such as Dr. Root and Dr. Rea.

And of the forth pilot study that we propose, one is detoxification. And we would mention that this is evidence-based for certain exposures and certain chemicals. For example, there are control trials of workers exposed to things like polychlorinated biphenyls where they've actually used this detoxification routine which is published and well-defined, and shown that the group that underwent this routine, eliminated the PCBs from their bodies more quickly than the other group.

Another thing that we propose, is the old-fashioned way of assessing people for this so-called avoidance routine, and the old- fashioned way is the person who lived at home and they saw a physician trained in things like elimination diets and avoidance of chemicals, trial and error. For example, the old-fashioned way was, "Why don't you turn off your gas stove for a week and use a hot plate, and at the end of the week, turn it back on and see if the . . ." We know that gas cook stoves have sulphur dioxide, oxides of nitrogen, and so forth, that are higher than the levels allowed in factories, so see if the fumes from an unbidden gas appliance might be the factor in your treatment. So a group of veterans could undergo this type of home-based elimination routine. And then, we would propose sending a group of veterans to a clinic that uses the detoxification routine combined with this challenged avoidance technique, and test that. Another thing we thought of in terms of intolerance and elimination is to take a group of veterans, and some of the veterans with Gulf War syndrome are on a symptom-based. "There is a pill, if you complain enough today, I'll write a prescription." And it's been described that some of these patients are on as many as forty medications. What we would propose as a double-blinded drug

elimination, to take some of these poly-pharmacy patients and give them sugar pills, placebo-controlled, you can get a number of these drugs from the manufacturer with no active ingredient for these trials, and actually see to what extend this poly-pharmacy -- we know all drugs have side effects and things. For example, Jim Sullivan of Dallas, described a multi-drug intolerance symptom, whatever. We know that people who have intolerance for one drug, have a higher probability to having intolerance to other drugs, at least in some people's studies. So, that would be our short-term. Look at these four groups and see what we get.

Now, for the long-term, and this, I think, would depend to a large extent on the results of the short-term studies, we should suggest, that if this looks like a promising therapy for Gulf War syndrome, that there be the construction of one or more of these environmental control units. You heard Dr. Claudia Miller talk about this type of approach to medicine and this was a technique prescribed by Dr. Theron Randolph some 50 years ago, where he operated what he called an environmental control unit, the philosophy being that, as we all know from the EPA's team studies, everyone in our society is exposed to what has been called a chemical environment, and this is these low-levels of volatile organic chemicals, from out-gassing and so forth, the average American home, school and office, according to the team study, has more than a hundred, several hundred, volatile organic chemicals in the air, including pesticides, some of which have been banned, and so forth, at low levels. If you add it all up, maybe it's a significant level, and the hypothesis that's been advanced, that chronic inflammatory conditions and other conditions can be made worse by this chronic low-level exposure to chemicals, and that some people develop an intolerance to this level of chemicals. I think Claudia Miller defined that theory in its current reincarnation as the TILT syndrome, or the loss of tolerance syndrome. But this looks like a promising approach. These facilities should be made so that patients can go there and get these treatments, the detoxification. And I might say, detoxification may not, for this group of patients, may have efficacy for other reasons that you've eliminated chemicals from their body, because a lot of the chemicals that the patients were exposed to in the Gulf theater, are not things that are stored in fat and stay in the body for long periods of time. People have organophosphate exposures, for example, as far as I know, can have chronic symptoms, but there is no organophosphate left. And there might be other mechanisms by which this intensive exercise, vitamins and sauna routine benefits health. In fact, these things have been recommended universally, for years, vitamins, exercise and saunas.

So, we don't really know, for this group of patients, why it may help, it may be elimination of toxins and it may have other benefits beyond that, but that's our recommendation.

Dr. Kristina Dahl

The pilot study that I like the best is the sauna detoxification program and the reason for that is, if I've ever learned anything from Dr. Natelson, it's that research should be evidence-based. It's not just one, but there are many studies, that have shown that groups of people who have been

exposed to various chemicals and have gone through this program, have had reduced amounts of chemicals after that, especially in fat biopsies, with concomitant reduction or elimination of symptoms. So I think, in my own opinion, that's enough to justify a pilot study. And I think, yes, of course it would be very difficult to double-blind a sauna program, but you might be able to do something like reverse the order. If it's important for the patient to exercise before hand, have one group have the sauna beforehand, if it's important that they get the oils, give them something else that looks like oils, or don't give them the niacin. So I think there might be ways to partially blind it. Although, it would be nice to have a control group who weren't treated at all, as well.

The other point I wanted to make, well you've made it already, is about patient selection. I'm not an expert in this area, so I don't really know which chemicals are stored in the fat, that the Gulf War veterans have been exposed to, but what I would look for is something that they have been shown to be exposed to that is stored in the fat, and look at that one thing, to start with. So the veterans are a heterogeneous group, so if we pick some that we know have had a certain exposure and we look at levels of that particular chemical, well we're not going to know about everything else, but at least we can learn about one thing.

Dr. Benjamin Natelson, Chair

Can you tell me, what study has done toxin fat biopsies, just so I get some sense, because I don't know this literature.

Dr. Kristina Dahl

Actually, Dr. Root knows this much better than I do, so why don't I let him talk about this?

Dr. David Root

The initial study that was done in, it must have been about 1978, used PCBs and PBBs. It used seven subjects from Michigan. Those of you in occupational medicine may remember the debacle when there was a mix-up in a food additive for cattle, and it was mixed with a PBB fire-retardant chemical. And most of the people in the state of Michigan and surrounding states got a pretty big dose of the polybrominated biphenyls. Seven of those individuals were tested using fat biopsies before, during, after, and then four months later. They were looking not only at PBBs, but PCBs and also some of the halogenated hydrocarbon pesticides. Sixteen separate chemicals were looked at and all but one of the sixteen came down from anywhere from about, I don't have the exact figures, but anywhere from about 16-30% reduction during treatment. Then they thought, "Well maybe all we've done is rearranged the stuff in the different body compartments." So, they brought them back four months later after treatment, and low and behold, the numbers had continued to decline. So, the point being, we not only need to test before, maybe during and certainly after treatment, but we need to test four to six months later, to do the same testing that

we're doing.

And I'd like to make some suggestions on the detoxification program. At my office in Sacramento, I can probably handle about twenty patients a month, using two saunas, two bathrooms, and so on. What I would suggest is, because this program can definitely be replicated at VA facilities, all you have to have is a sauna and a shower, a place where people can change clothes. Right now, at my clinic, I have one sauna and one bathroom and men and women use it, and we don't have any problems. So you can use one, but we will have two shortly. During those first three months, twenty a month for three months, I would recommend that we bring people from appropriate VA facilities, whichever ones are chosen, to train, because there's going to be a significant amount of training for the staff who's going to be doing this program at other facilities. I think there's a real need to demonstrate that this program can be replicated.

So, that would be a really strong recommendation of mine. And then, certainly, on in-take, we should be very careful, because there are certain conditions and we should not put people through the detox program if they have those conditions. One of the main ones is pregnancy. We cannot treat women who are pregnant. People that are on massive doses of medications, we're going to be eliminating those at a rapid rate and we have to be careful with brittle cardiac status problems. We have treated diabetics with insulin dependency so we can deal with most of those problems, but we have to be very careful on medications. If we have some idea what the individual has been exposed to, I think we should definitely do fat biopsies which we can do using the needle technique, I've done it, I'm trained in it, in the rump. If we need more than that, if we're going to look at the dioxins, we're looking at 10 grams of fat and we'd have to do incisional biopsies.

I think there are some other things we might want to look at. I would not exclude patients with DU exposure, because we know that this treatment program can lower the body burden of several metals, including cadmium, mercury and lead, and my radiation physiologist tells me he thinks very certainly, we can mobilize some of the DU in the body stores and probably see some reduction in total body burden of this. And that's something that I think should be looked at. We might want to look at chromosomal studies to see if there are any cystic chromatal changes, we certainly want to do immunotoxicology testing, neuropsych testing and a few others. So, I would suggest we look at it as sort of a short-term but training other teams from selected VA hospitals, so we can get this out into the system and allow, assuming that it's going to work, and I have no doubt in my mind that it will, that we'll have some facilities set up where we can put more and more people through. I'd be happy to answer any questions.

Dr. Benjamin Natelson, Chair

I think this makes a lot of sense. I think that what I'd do before I threw all the babies into the bath, is pick one or two VAs, one or two sites. You're doing it, after all, with one sauna. This is simple, this is, if it works outside of Dr. Root's hands, we're going to see it work quickly, and

that's great. It's not going to be controlled, but then, after all, a little bit of–it has the same flaws as our drug studies – they're open label. And I think it's reasonable, in a small way, to look at it because, again, the data of the veterans. I think 12, 15, small. Look, this is a pilot study. What Dr. Root is telling us, that tall gentleman, the three of them, they said it was night and day. I mean, that's the sort of thing a doctor can believe pretty fast. So, you don't need 200, if it's night and day. You need 200 if it's 11 o'clock and 12 o'clock, if you know what I mean.

She's just designed the trial. You have your 15 or 20 people go through that are pre-tested by someone who's not in your group, and the problem here of course is to brief the subject, and it's very hard, not to give any hints about whether he or she was treated or not. So, you might try to even blind it by putting them in the sauna but only turning the sauna up to say, 80 degrees. Heat could be a variable. You probably need it to be, I don't know, 100 degrees, whatever, so make it 70. That would be a good way to do it. Because one of the things that's very powerful, is we are very powerful doctors and putting someone in the sauna for treatment is very powerful, so I think you could do that and try to get, again, the sorts of things we tried to get with the drug trial, some measures of outcome, and here the idea is to blind it in some way. I do think you could use heat as a dependent variable, though.

Dr. William Meggs

Some of the assessments would be, for example, filling out a questionnaire on neuro-psychiatric testing. Even the person who scores them has no idea where they came from.

Mr. Anthony Hardie

I'd like to ask, from the veterans' perspective, for those folks that were at the Veterans' Forum last evening, there's an awful lot of anger. And that anger is starting to get redirected into, "We don't need more research, we need treatment." Now as I'm hearing you talk about a blinded study and so on, and only twelve people participating, this seems like one of those studies where it would be very easy to conduct having 200 people in the study, not blinded and using the before and after results, measuring everything that's coming out of the participant's body, you're going to have a before and after, you're going to have a very subjective point of view from the patients perspective as well, of has this helped me, has this not helped me. And to do this, starting in three weeks. Starting it very quickly. This may not be good science, this may not be from the scientific paradigm, however, it's going to make a difference for veterans and the folks you saw last night is representative of veterans. We have 200,000 vets out there that are feeling the same way. Let's do something out there that is not double blinded and if there is a precedent for this, it's during the AIDS crisis. There were some studies that were done that were not double blinded, simply so the people could get the treatment as quickly as possible, to see if it did, in fact, make a difference.

Dr. Nancy Fiedler

I think that's a good point. Let me just add one thing that I think could be a compromise. That is, there is such a thing called a waiting list control group. And that means that you might run the study and it might only take three months to run, and you might even do maybe more people, but when you get the first results out, the people who were the control group immediately go into treatment. So that way, you're not really withholding treatment, because you really couldn't treat all those people at once anyway, there probably wouldn't be the resources. You still get your control and you still get everyone treated, and you know something about the efficacy. So, I think it's a well-taken point, but I think there's a way to do it and satisfy both groups.

Dr. Benjamin Natelson, Chair

I think Mr. Hardie, the question here is do we want to push a start button that gets 200 vets started, or do we want to push a start button that says let's get started with, instead of three giant steps, two smaller ones, because we're going to see very quickly, in a very short amount of time, if it's Noon and Midnight, or Noon and 12:30? If it's Noon and 12:30, it's still studyable, obviously. I hear you. I'm being a researcher and saying, let's start it and see it, before we say it's the only thing we're going to do. They came up with four ideas. I guess, if that was the only idea we wanted to have come out of this, we could go in a bigger way. The other thing you have to understand is, we're giving them our ideas and someone's got to pick it up and say they want to fund it. The Congress has asked the broadest public interest, which is us in this room right now, to come up with a set of ideas and possibilities for current and future research. Once we've done that, we don't know who's going to say we want to do this study. So the idea is the crux, not the number.

Mr. Anthony Hardie

I think that the idea of the waiting list is very important. And as well, being a realist, you're going to need to find volunteers to do this, and I know it's going to be very difficult to find volunteers to do this. We're already having a difficult time managing our lives. To find people who are going to want to volunteer in a time-intensive study such as this, is very different than taking a pill. [Disagreement from the audience].

Dr. Dan Clauw

I'd just like to make a comment. I think that perhaps the strongest recommendation our group needs to make is, if any of these projects that we recommended today are to move forward, there has to be a different review process than the process by which grants are normally funded. As being both a reviewer and reviewee, nothing that we talked about today could get through the standard peer review process. So, one of the things I think we need to consider recommending as

a group is that there be some sort of request for proposals, and a special review committee that understands the urgency of the needs of the Gulf War veterans with respect to these treatment studies, and that these are somehow streamlined and done differently, because we had for our big exercise in cognitive behavioral therapy trial, we had difficulty getting that through the review process even though there was incredibly good empirical data supporting the fact that these were efficacious interventions. So, everything else that we've done today will have been a waste if we don't come out with some sort of statement saying that for these types of projects, there needs to be the equivalent of what the NIH does, with a special emphasis panel, which you know very well. With certain diseases and certain problems, the review process has to be somewhat different, and it has to take into account the fact that there won't be pilot data to support some of the things that we're proposing.

Dr. Benjamin Natelson, Chair

If Congress is on our side, if Congress says they want it done, it's going to get done.

Dr. Dan Clauw

But even now, there's a law that was passed last year, that everything for Gulf War illness has to be peer reviewed. So this is Congress, this is VA, this is DoD. Everyone has to sign off on the fact that this is a problem that's going to require some sort of different review process.

Lea Steele, PhD
Director
Kansas Persian Gulf Veterans' Health Initiative
Arlington, Virginia

I'm with the Kansas Persian Gulf Veterans' Initiative and I also have another hat, and in that hat, I am on the Advisory Board for NIH's Office of Alternative Medicine, in which we look at quantitative methods that can be applied to research and things that are difficult to research, specifically things that don't lend themselves well to either double-blinding or placebo controlled trials. Things like massage therapy and acupuncture–you can't really double-blind or placebo control. I think some of the things that have been brought up here are in the same category, and I think if part of this body's effort is to make some recommendations, you might also include the fact that there's substantial literature that already exists in terms of white papers, agency reports and peer reviewed journal articles that address these kinds of issues. For example, if you consider a randomized double-blinded placebo controlled trial to be the gold standard of how we assess an intervention, one deliberative body that I was a part of came up with the notion that, actually the most essential ingredient in this is randomization. You can make due with the other components of that. That's just one example. There are a lot of things that have been sort of carved out, including things like study sections that peer review applications for intervention studies that

aren't conventional, that assess things that don't lend themselves to pill giving and double-blinding.

Dr. Vinh Cam

As a follow-up to what Dr. Clauw just mentioned, I really think that's the way to go. Find some expedited review and still come up with a quality review without going through eight months of RFP. From my side, I would try to make that recommendation to our own vehicle. Another point is in order to get an expedited review, we might have to prioritize that research and that's kind of a compromise. I don't know whether it's possible to put all these four as equally important. So, I just wanted to mention that.

Audience Member

I had the treatment that Dr. Root was talking about – the detox program with niacin and supplements and so forth. I can't say it cured me, I'm still getting worse, but it did slow the progression. I was getting worse real fast, and I stopped getting worse real fast and started getting worse slowly. But I want to say that my doctor told me I would feel worse afterwards for awhile and it would take about six months for my immune system to calm down after getting the toxins out of my body. I didn't believe in any of this stuff. I just went because I didn't know what else to do, and it actually happened exactly the way he said it would. The point to this is, please don't assume that everyone is going to have magical results right away. It can take awhile for the immune system to calm down.

Dr. William Baumzweiger

I didn't hear anything about the disautonomia study we were talking about.

Dr. Benjamin Natelson, Chair

We're not done. We're done for today, but we're not done. We have done a lot. It is 5:30. We are within target. What I'd like to do is, we're going to break. I'd like to ask Drs. Gordan and Clauw to just stick around with me so that we can just come up with this last piece.

What's happened is we've done a lot of work today. We've come up with targets. I think what I'd like to do in tomorrow's morning session, is I'd like to be sure we're all on the same page. With these four studies, do we want to A, B, C and D them? Because what we tried in our little group, was to narrow it down to two areas, now maybe three areas of potential trials. So, I think we'll spend a little time doing that, and then I think we're almost home, because we'll just lay these out. What I'd like to do is try to compress these a little, well, that will be up to the workshop, whether we compress these to like, two suggestions, a short-term and a long-term

from each of these, because again, there are four of these; that's a lot. Or, do we just leave it as a pretty big, open document? So I need you folks here to think about is there a way, can this be further compressed, and you folks, can yours be further compressed?

Audience Member

One of the things that I'd like to have before we go home is approximately two pages worth of something, and I don't know if you want to charge your subgroup chairpeople, or maybe that's what you've just done.

Dr. Benjamin Natelson, Chair

Well, I think I have. What has to happen is, I thought that we would get a chance to do that tomorrow, but you think we need to do that tonight? It would probably be reasonable. I'm going to pick then, Mike, Dan, Bill and Stu. I've got to ask you then to prepare a brief of up to two pages. Basically it's going to be much shorter because -- now, this is going to have to be viewed as penultimate, because tomorrow, I'm going to ask you to project this information that you have, we're going to go over it one more time, and then we'll put it together.

Dr. Vinh Cam

If we want all our wish lists, maybe we can just come up with one item and list it as therapy/treatment, and list all this. Then people just vote on one item.

Dr. Benjamin Natelson, Chair

I think it's probably reasonable. I'm trying to be efficient and give them something that they won't forget, you know? I think that from this workshop, if they got six pages as opposed to two pages, that would be fine. So, that's the tasks. If anyone in the audience is unhappy, then it's time to come forward before people disappear. Thank you. We'll see you in the morning.

The session was adjourned.

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Day 3 – Tuesday, March 2, 1999

Dr. Benjamin Natelson, Chair

What all of the groups have done, is to work last night to get something down on paper so that we have something to discuss and see where we are, vis a vis, the needs of the veterans, the needs of other members of the audience, and the scientific issues that the panel is supposed to be dealing with. So, let's start with the first document, which is the pharmacological therapy, and Dan, why don't you lead us through it?

I think that there are two major points that we need to talk about. The first point is that since these trials are very focused towards a specific problem, to get them funded will require that they be evaluated as themselves. That is, that they not be put into a straight peer review program, because they won't get approved, and that's a problem. The purpose of this meeting is to lay out a way to deal with the symptoms and problems of the Gulf Veteran in such a way that we can get these trials set up. So, step one is critical, in that special peer review panels need to be assembled. Dan, what was the second point?

Dr. Dan Clauw

I talked to Wendy Wendler last night, and one of her concerns was, and I think it's very legitimate, was that as research progresses, if we identify specific subsets of individuals with Gulf War illness that have a specific treatable problem (i.e., mycoplasma that could be treated with doxycycline, strep that can be treated with Dr. Hyman's protocol, then this type of testing should be done to symptomatic individuals to see if they have those problems, so that they're not treated as being an unspecified chronic fatigue, fibromyalgia type of case. So again, I think the other thing that this helps with a little bit, and this is my personal opinion, perhaps we can bring it up for discussion. I think that suggesting testing of all symptomatic veterans, such as SPECT scanning, that does not lead to a specific treatment, SPECT scans are abnormal in a whole variety of conditions, and finding that someone has an abnormal SPECT scan doesn't in any way help you treat that individual as a clinician. Those types of testing, I'm not sure are the kinds of tests we should be recommending for all symptomatic veterans.

So anyway, this second point was, as research progresses in Gulf War illness, if a subset of Gulf War veterans have a specific cause for their symptoms and an appropriate treatment, for example, an infection and an antibiotic, then this testing should be considered for all symptomatic veterans.

Ms. Wendy Wendler

Great. But infections can be fungal or viral . . .

Dr. Benjamin Natelson, Chair

Anything. His point is that Gulf War syndrome is a syndrome. And as soon as we find a cause, say we find bacteria X does it, well obviously, we want to test and treat it.

Ms. Wendy Wendler

And concur it with other causations. It would really be just normal as part of related conditions, it says in your original . . .

Dr. Dan Clauw

Exactly. The things that we're talking a lot about in treatment is treating non-specific symptoms. But what this gets to is that if we identify that a subset of people with non-specific symptoms, has a specific problem that we can treat, that obviously, we do the testing and we do that treatment. We don't lump that person into a treatment trial for non-specific chronic fatigue.

Ms. Wendy Wendler

And we can even screen to rule out part of the research for something else, because we don't want that to clutter up. While I've got the mike, we were concerned about the pain suggestions, too.

Dr. Benjamin Natelson, Chair

Well, let's see. There seem to be two overriding things that we want to get, just to review, that there be appropriate, directed, peer review that would review who, and does this work, and number two, that when causes for the syndrome of Gulf War illness is found, that veterans be tested and not included in the group of Gulf War illness any more, because they have a cause.

So, the short-term idea is an open label, and we're being vague here. We're not going to lay out the specifics of any trial. So what we laid out here is an open label trial, looking at low doses of tricyclics, venlafaxine, and the tramadol. Those are examples of which would be doxepin, Effexor, and Ultram, because those are usually used in the physicians' armamentarium of moderate to severe pain and headache. So, that's the first. And then, cognitive symptoms, again, a trial examining the efficacy and the Wellbutrin and Cylert, although we did hear from the audience, questions as to whether Cylert really will be efficacious. It has been used in multiple sclerosis and it seems to be helpful. So that would again, determine whether these medications have efficacy in Gulf War illness. What we've done here, is try to pick two problems that the Gulf Veteran suffers from, and this could begin very quickly. The one thing that's missing here, though, are the vehicles and I think we ought to get the vehicles in. So, I think that what you may be putting in is

the vehicles to assess improvement. They would be pain vehicles, quality of life, symptom severity and veteran satisfaction. Again, we're not going to specify the vehicles here, but we're going to give whoever looks at this document, some idea of what we think is appropriate.

Someone in the audience was concerned that this would be a protocol where, if they were not in, whoever was funding this, they would not be able to get access. But in point of fact, you would, because the design would be available, and your doctor could do it, and your doctor wouldn't necessarily have to do the outcome variables, although it would be useful to have, to see if you got better. Comments from anyone about that?

Panel Member

I'd just like some clarification from the Chair. If we're going to immediately conduct these trials, are pain and cognitive symptoms what we're giving examples of what we can possibly treat, or is it going to be taken that those are the two symptoms that we're going to be locked into?

Dr. Benjamin Natelson, Chair

Well again, I don't know how to answer that question. What we wanted to do was get something really concrete down there. Now, I think we could say, and I have no problem with this, I'd just have to caucus with my colleagues, we could say that other treatable, specific symptoms, similar open label studies should be tried on other treatable symptoms, and an immediate one would be headache, which might be different from systemic pain. So, we could put that in, but again, I was a little afraid that that would water things down as being sort of a white paper, and here, I wanted to be specific.

Dr. Dan Clauw

What you find in clinical practice, I think, is that fatigue and cognitive difficulties tend to parallel one another, and the medications that you might consider using for fatigue overlap significantly with the ones we have up there for cognitive difficulties. I think the reason we thought we could study cognitive difficulties is that it's a little easier to measure more objectively as to whether people improve or not, whereas fatigue is a very sort of nebulous thing to try to measure as an outcome variable. We do it, we ask people how their energy level is, and how they feel, but I think all of us acknowledge that it's more difficult to measure fatigue than it is to measure pain, or than it is to measure cognitive symptoms.

Panel Member

The only thing that I'm concerned about, and I'm sure that you can hear what it is, is that the format is really appropriate, the N of 1 trial and the way you have it stated, I'm afraid that we're

going to be locked into using those specific drugs and maybe that's a good thing. I don't know.

Dr. Benjamin Natelson, Chair

First of all, we don't have the design here and maybe we need to think about addressing it. We can come back to that. We're not really talking about N of 1 trials here. We may be talking about a small open label trial, of pre-post data. I think N of 1 would probably be the best way to do it, but you could quickly run 20 subjects through a sequential study and look at the group effect too. Why don't we say after "Vehicles to Assess Efficacy or Outcome" the above could be considered a model for evaluating other focused symptoms. How's that?

Panel Member

I think that's good. One suggestion that I might make is a really good assessment for pain inventory is the multi-dimensional pain inventory, the MRI.

Dr. Benjamin Natelson, Chair

You mentioned the NIS. I don't think we need that kind of nitty gritty here.

Panel Member

I don't either. Are you saying that somebody does their own independent little trial, and then we have this own little trial over here, and then over here, as we put this data together, or the idea of that Gulf trial network seemed to be the most efficacious kind of model.

Dr. Benjamin Natelson, Chair

We don't know. Again, we're sort of tasked, I think at the end of this morning, we'll have some sense, but I think what we're trying to do here is get down on paper the ideas and then the execution is going to be the next problem. That's not on our plate, the execution. So I think it's a mistake to worry about it now, and that what we want to do is sort of drive through this and make sure that we're relatively on the same page, that everyone is comfortable, and go from there.

Panel Member

Could you sort of make us happy and put something in there? What I'm afraid of is, in the future, we're going to say, well, this was just a recommendation to do these studies on Ultram, and in fact, yesterday, you said that in no means do we stop here, that we have to go further. However, I'm worried that they're going to say, "No, we don't go further because it was recommended to

us by the panel at your own Conference." Is there any way we can put in there that, by all means, remember that the need for further pain medication is always a possibility?

Dr. Benjamin Natelson, Chair

Sure. That's easy to deal with. So then, back before the "Above" let's say "Subjects still suffering significant amounts of pain or cognitive problems at the end of these trials, shall be considered for subsequent trials, using other available medications."

Dr. William Baumzweiger

You could put calcium channel blockers in there for headaches. Right?

Dr. Benjamin Natelson, Chair

One of the things we could do, the way we deal with that Bill, is this sentence. Say you go through this trial and headache is still a problem. The idea that you expressed that headache and body pain may not be susceptible to the same treatments, instead of our stipulating everyone, what we have done is we have achieved trials. We have not closed the book on other trials. We are being concrete, and we have also given examples of what to do if people are still sick at the end of the trial.

Ms. Wendy Wendler

The phrase that these trials would have to be done, what if there's already some sort of existing data or material that Ultram doesn't do diddly for me, could we propose more things without having to wait?

Dr. Benjamin Natelson, Chair

The issue is, that in a trial, there are two ways to think about a trial. I like to view a trial as, does a treatment improve the whole body of people with Gulf War illness? So, one person may not improve, but the group as a whole, does.

Ms. Wendy Wendler

I've talked to a lot of vets. I've been doing this since 1993, and I hate to tell you, I sort of know the answers to some of these, if you ask the vets who have the pain. If you ask Joe Poe you'll have to do a trial on some of this stuff because we are the data, we're two-legged lab rats. There's a phrase "Already existing data or materials to proceed in other directions."

Dr. Benjamin Natelson, Chair

Well, we can say that, that's not a problem. Again, if we can develop some way of systematizing the information that you have picked up with this sort of website stuff, that would drive the design. We could say, anywhere, that the drugs suggested would be. . . the problem is you don't want to water this down, Wendy, that worries me. We've got something concrete here. As soon as I start saying that the drugs recommended could be changed per available knowledge, I mean, I don't have any problem saying that, by the way -- we're going to learn about the set of all because the Gulf veterans that I see, and care for, many of them are less severely ill and disabled and do fine with this kind of regimen. So again, this is a regimen to try. This seems reasonable as long as we keep the door open to other trials. So you're saying other trials can be done for people who are resistant . . [Simultaneous discussion].

Dr. Stuart Brooks

Why don't we say, "Subjects still suffering significant amount of pain or cognitive problems at the end of the trials, shall be considered for other available medications." [Simultaneous discussion].

Dr. Benjamin Natelson, Chair

Okay. What we need to do is make it for individuals who have not been tried on the medicines. Individuals who have been put on these medicines, and who have been tried on Ultram, it would be ridiculous to put them into a trial with Ultram. So this is a trial for individuals who come in with untreated, unexplained pain. Maybe we need to stipulate that. So let's say "An open trial aimed at veterans with untreated pain." What we're trying to do here, it seems to me, is to get a trial going on a way of, how do you deal with this problem?

Mr. Anthony Hardie

I would really like to see some sort of a survey before even getting into this, on the general points, but some sort of survey of veterans, of what we're doing already that is working for us. So we have situations of what is working and what's not working. That would be a really good starting point. We don't have a real good knowledge base of what we've tried and what we haven't yet.

Dr. Benjamin Natelson, Chair

I guess the problem is, those of us who care for veterans and do research on veterans as well as civilians with similar illnesses, know the literature that's out there, and doctors in practice are doing a number of different things and we're trying to come up with a systematic way of a trial. I think we're jumping into a lot of nitty-gritty without seeing what the other pieces are, and that's going to be hard. Maybe we should do the following, it's up to you all. Let's go through

everything quickly, so that we have a sense -- go ahead, please.

Ms. Denise Nichols

I'm a retired Major, nurse, not functioning as a nurse now because of memory problems, but I can still ask for resources when I need them, and read. I've been working trying to get Dr. Bill patients, people with insurance that can get to him, that can get some help. They have improved with his care, it's not a cure, I don't think there will be a cure for a long time, but he has improved the ability of people to function and try to maintain some kind of job, because we are not getting our compensation claims through. I've got people who have been given six months to live that have been denied their VA claims, that served 20 years. Yes, they're getting their retirement, but they're not getting their disability. I have a son that was military, that quit to take care of his Master Chief, Navy. I told you all, this is real. How many of you are neurologists? One, okay. Have you truly given each of your patients you have seen a neurological exam, just as I was taught out of medical books? Have you noticed the changes sitting and standing on our pulse rate? One thing, have you noticed how we can not differentiate where the sound is? These are real neurological damage cases. We need to stabilize them, we need to give them calcium channel blockers, we need to try to calm down the brain stem. This is critical. And I'm going to look you in the eye, Sir. I was a nurse. I served this country, as our other vets did. And we've been out of here eight years trying to keep living. And we're not going to die. We will come in wheelchairs, litters, every which way, and we will build in numbers. We've already built in numbers since the NIH conference. You are not doing anything different in what you're saying than what's been done in the VA hospitals – give them pain med, give them antidepressants. We are not . . .

Dr. Benjamin Natelson, Chair

Well I guess we have a problem then.

Ms. Denise Nichols

Yes, we have a problem, because you don't have any studies on calcium channel blockers . . .

Dr. Benjamin Natelson, Chair

Wait one second here. Let's back up. Do we need to have a study on calcium channel blockers? Why, Ms. Nichols do I need to put up -- let's go down to the bottom. We have put "Consider a trial testing the idea that neurally-mediated cardiovascular changes may be responsible for symptoms" and then we put down a list of treatments. I've discussed this with Dr. Baumzweiger. I do not believe that we are at the state of knowledge where we can be more specific than that. I think it's a mistake. If we do that, we are going to be putting handcuffs on future planning, based on inadequate knowledge.

Ms. Denise Nichols

Sir, treating them with pain medication and anti-depressants, like has been done in the VA hospitals, is not helping these vets to stabilize even their pulse rate. What we are finding is, the vets who have a greater pulse rate difference from sitting to standing, are the ones that are getting violent, don't even remember what they've done, and are in jail. And they were brave Americans, sir. They served their country.

Dr. Benjamin Natelson, Chair

Can I get some sense from other veterans? We're stopped here.

Ms. Denise Nichols

Well, I'm sorry, but you've got to move faster. We've got to get treatment.

Dr. Stuart Brooks

I think you make a good point. The question is whether pharmacological agents are going to be the answer, or non-pharmacologics. Some of these other proposals, some of these other ideas, maybe some more innovative treatments. The problem with pharmacological agents is that there's always side effects and other things that relate to it. There's a whole . . .

Ms. Denise Nichols

Sir, let the vets decide. These are going to be research studies, we have to sign an informed consent this time, not like when we went to the Gulf with PB.

Dr. Stuart Brooks

I understand that. But, that's one aspect of the pharmacologics, and I think focusing now on what drugs, types of drugs deal with the experience of the audience, really doesn't get to what we're talking about, a treatment trial or a drug trial that will be one in which we can look at in a research manner.

Ms. Denise Nichols

We'll look at it, but I'm asking you all to move it up, make it a research project, please Sir. You haven't visited these vets that are now in jail, that were brave patriotic individuals. You haven't seen their face, sir.

Ms. Venus-Valery Hammack

We need to try different remedies in these trials. That's the object of making new recommendations, and if you're avoiding changing pharmacological protcols -- I have to say that it sounds like great fear in changing and modifying, going to additional new protocols. We are not saying this is a standard treatment. We must try different alternatives.

Dr. Benjamin Natelson, Chair

We agree with that. We can strengthen this statement. Instead of saying we consider, we can say we recommend . . .

Ms. Denise Nichols

We recommend immediate, fast-track of a trial, actual research project, use those strong words. You don't say consider, sir.

Dr. Benjamin Natelson, Chair

We recommend strongly, a trial testing the hypothesis that neurally-mediated cardiovascular changes may be responsible for symptoms in some persons with Gulf War illness. Then we're going to give them the sort of standard list of therapies that can be used, including calcium channel blockers, which I think is a neat idea, because . . .

Ms. Denise Nichols

Can we put a time period on it, within six months to a year?

Dr. Benjamin Natelson, Chair

We certainly can, but, let's move it up to short-term and let's put the timeline on the short-term. That will take care of it, it seems to me. So, let's move that up there, and let's be specific. So, short-term is going to be within the year. How's that? It seems reasonable. We could say "Now" but practically, within the year.

Mr. Anthony Hardie

Could we use the word "urgency?"

Dr. Benjamin Natelson, Chair

Yes, sure. Let's put that in the first -- consider certain studies . . .

Mr. Anthony Hardie

I'd like to recommend that before we take any more comments from anyone, panelists or veterans or whoever, that we just go through the entire thing first and once we get through the entire package, we understand what everything is, then we'll all have lots of comments.

Dr. Benjamin Natelson, Chair

I think that's eminently wise. So let's plug down and do that then. So long-term, the two long-term ideas are getting data for hypofunctioning endocrine glands and those would be tested with low dose replacements, by using appropriately controlled trials.

The next piece then, is this idea of looking at the nutritional supplements and vitamins and again, using this as a launch pad to test them, because no one else is going to have the funds to do it. Let's go on to the intolerances.

Dr. William Meggs

These are treatment regimes based on Intolerances, and we heard Claudia Miller talk about the toxicant-induced loss of tolerance theory, where people exposed to high doses of chemicals develop a loss of tolerance to a lot of chemicals. We actually have a mechanism of this pretty well understood in the airway, where Dr. Brooks talked about asthma and people with rhinitis and sinusitis. So there are reports of veterans who have this toxicant- induced Loss of tolerance and get relief by reducing the chronic exposures to irritants that people have in their homes and workplace and so forth. Along with that, it's thought in some quarters that people store chemicals in their bodies and they can get low-grade symptoms from the chemicals stored in their bodies and routines have been advocated to eliminate toxins in their bodies, detoxification schemes. Detoxification is a treatment which says intensive sauna baths, stringent exercise and certain vitamins, such as niacin are given to increase the fat mobilization in the turnover of chemicals. So, the intolerance treatments are based on eliminating chemicals from the body and eliminating chronic exposures from chemicals.

We propose in the short-term, that we fast-track some studies and these studies should be undertaken immediately. The workshop proposes four pilot studies. Now we suggested that it would be best to control these, but we think in the interest of efficacy, either they should just go ahead and do some uncontrolled studies, or have waiting lists for controlled studies so that everybody enrolled gets the treatment. Some people may have to wait a month, some people have to wait a month anyway, because there's not the facilities to induce these.

We think the patient selection is very important. It should be patients meeting Gulf War syndrome criteria, if you have the multiple-symptom complexes, but most importantly, the cerebral symptoms, with the cognitive dysfunction with the loss of memory, and respiratory and muscular and skeletal symptoms. Or short-track it. The way we propose short-tracking it, is there are clinics in place now, doing these treatments. Let's go on and send some veterans, tomorrow, if possible, to these clinics and run them through the routines that are in place and are treating veterans and anecdotally having good success. We've identified a couple of clinics, and although we don't name them, behind the scenes we will be suggesting that.

For the four studies, one is detoxification, the other one is avoidance, and this is done in two ways. One is clinics that have special housing that have reduced levels of irritants, combined with detoxification, see how that does, and there's a low-tech approach to avoidance, where people just work with their physicians. They make changes in their home environment, they create a room that has a lower level of irritants, maybe get rid of the acrylic carpets and just use electric heat, or whatever, and this has been described in the literature. The fourth thing, it's been suggested that some veterans have been treated with poly-pharmacy, where, for every symptom, somebody writes out a prescription, and in one study of veterans with Gulf War syndrome, some were on 40 different medications. This seems incredible to me, and the max found in the study was 250 prescriptions in the medicine cabinet. For these symptomatic drugs, we thought you could do a nice little trial by just taking people off all drugs, and see if that alone might improve some people. Clearly, we're not suggesting that people with diabetes go off their insulin and people with severe hypertension go off their anti-hypertensives, but we're talking about purely symptomatic drugs prescribed for this condition.

Over the long-term, we suggest that one or more treatment centers to use these modalities be set up for veterans, which would be available for veterans who need it. Of course, this recommendation would depend on the efficacy of the pilot studies. If we see that these things aren't helping, well, let's not waste the money and let's not do it.

Mr. Kirt Love

I would like to see, if it's possible, a veterans' advisory committee, composed of Gulf War veterans, to some way or another participate in all of this.

Dr. Benjamin Natelson, Chair

You're going to see that in this macro piece. The next is non-pharmacological therapies.

LTC Charles Engel

The initial introduction sort of provides some brief rationale for what we're trying to do. It

basically states that whereas pharmacological strategies are easier to integrate into the usual process of care that patients receive, with non-pharmacological therapies, some of the obstacles of trying to implement them are the fact that visits to the healthcare provider tend to be brief and are oriented around the physician. What we have attempted to do is layout a framework in which non-pharmacologic therapies can be implemented in both primary care and specialty care, and evaluated.

The short-term recommendations, rather than focus on specific non-pharmacological therapies, we chose to recommend instead research of a more comprehensive and population-based approach to non-pharmacological care. The first step would be a needs assessment that would involve all Gulf War veterans including reservists, not currently covered under either the DoD or VA healthcare systems. This could be completed using some type combination of pencil/paper survey, semi-structured telephone interviews and/or clinician administered systematic assessments. The needs assessment phase would provide an opportunity for the VA/DoD healthcare system to essentially embrace veterans in a way that, as we have heard from veterans, they have not done historically, at least in the recent history as it pertains to Gulf War veterans. We recommend some areas of inquiry which would be used to evaluate the effort. Current communication modalities available for veteran healthcare information exchange, such as PC and Internet access, and so on, perceived need for health information, I say perceived, because one of the basic tenants outlined earlier in the proposal is that we feel it is important to emphasize the veterans' perspectives rather than our own.

So, we are valuing the perception above what other folks might consider a reality, I guess. The need for assistance with activities of daily living, the need for specific types of healthcare, access to care, barriers to care, which would include the benefits assistance process, levels of symptomotology of various sorts, satisfaction of care, overall quality of life and illness-related distress.

The result of the needs assessment would be an initial pre-care guided use of self-care strategies and this could be done in an evaluative manner in which a group of people could get a book that is general about self-help strategies for the sorts of illnesses and health concerns for veterans. Another group could get more focused targeted literature based on the results of their needs assessment and we can look at in that way, the added benefit of doing the more targeted assessment, and depending on how much more beneficial it was found to be, it might be conceivable that it's even less beneficial. I doubt that, but it's conceivable. We could then choose to implement one strategy or the other. Folks would be initially assigned to either routine primary care or a more intensified version of collaborative primary care, that would involve other members of the primary care team, based on the needs assessment, or based on their response or lack of response to the primary care approach. Outcomes would be assessed in a manner similar to the needs assessment, looking at the same kinds of variables.

In the next step, the final step, and it's important to emphasize these are all short-term recommendations, the final short-term recommendation would be that we would evaluate intensive specialized care programs for folks with chronic symptoms of various sorts; these overlapping syndromes that we've seen so much in Gulf War veterans–chronic fatigue syndrome, fibromyalgia, multiple chemical sensitivity, and the like. These would be reserved for the subset of veterans who either indicate through their needs or through their lack of responsiveness to the less intensive forms of care, and they are quite similar to the sorts of programs that are currently being developed within the DoD and the VA, which I think are important programs, but I would describe them as tip of the iceberg sorts of programs. They're only dealing with the most-severely ill and there's a whole bunch of other folks out there who are earlier in symptom progression and less ill, and we may be able to prevent them from reaching that stage of severity.

Under long-term recommendations, essentially, what the short-term recommendations focus on are modalities that are currently evidence-based and in use for analogous symptom syndromes to Gulf War illness. Clearly there is a need to evaluate and implement some of the other strategies that we've heard in this meeting, and I'm sure others that people will bring to the floor, in time, and there should be an openness to looking at those and running pilot studies. For those that appear most promising in pilot studies, develop a program of randomized clinical trials, so that we can determine their efficacy and implement them, broadly.

The second long-term objective is to develop a coordinated quality improvement program that encourages what in the field is called health services research, which is essentially quality improvement research, and research into innovate efforts to decrease these non-pharmacological strategies into the process of routine medical care.

Mrs. Mary Lamielle

Although he mentioned under intensive care for chronic syndrome symptoms, multiple chemical sensitivity, it's not on the list and I think it's critical. It's a list that says chronic fatigue syndrome, fibromyalgia and it does not say Multiple Chemical Sensitivities, and I insist that it be put on the list right now.

LTC Charles Engel

Actually, I think it would be better to put in MCS. The reason we didn't include it was because I wasn't sure how the folks adhering to the MCS hypothesis, would view some of the treatments that are available here. Let's get it in here.

Dr. Stuart Brooks

Okay, this is the Macro, and we wish to establish a central body, and we thank Joe Poe for the

acronym of LOK-N, what we call a **Lo**gistics Communication Networ**k** Ce**n**ter that will coordinate communication, education, outreach efforts necessary for the effective conduct of treatment trials and research programs for Gulf War-related illness. Furthermore, this body will facilitate communication channels between veterans, VA healthcare professionals, researchers, and administration. So, for the short-term, we would establish this LOK-N that consists of appropriate parties, and we mentioned some of those, committed to enhanced communication and outreach and education among groups as it relates to treatment trials and healthcare services. To support this concept and the adoption of these recommendations, the center may be modeled in a manner similar to the National Center for Post-Traumatic Stress Disorder. I mean, as an example.

Then for short-term, establish LOK-N with members of the administration, develop goals and operative procedures, first step may be to establish a central databank of completed and on-going research, part of that would be involving needs assessment focus groups, for both veterans and healthcare providers, establishing a website and newsletters and establishing a coordinator, who would be responsible for interfacing between the focus groups and lock-in.

Then long-term: conduct and develop programs and protocols and communication and various educational tools such as was previously mentioned, that might be centrally coordinated through LOK-N. The areas of research may include such topics as education of VA healthcare providers and staff administrators as well as the families and advocates. They can address issues such as needs assessment of potential applicants, identification and recruitment of candidates for study, communication through newsletters, Internet sites, self-help education, educational materials for various parties, examining the administrative processes that are indigenous to the veterans' care, ones that may be stumbling blocks for high-level quality of healthcare delivery.

Methods: Identify and recruit candidates, update veteran's effective treatment protocols, develop outreach. The audits would be the kind that go out looking at quality of care and so forth, satisfaction, and attitudes toward Gulf War syndrome illness. Other ideas, we actually did a little survey last night, and communication with some of the veterans, establishing Internet site, updating primary care practitioners who are knowledgeable about exposure information, perhaps using occupational and environmental medicine expertise, directing interested veterans to clinical treatment trials, monitor availability of effective treatment drugs to be considered for compassion use, identification, dissemination implementation of therapies that are effective, match veterans with specialized care centers, treat veterans with dignity and respect. Some specific things that were pointed out to us were knowing how to code these things, whether available medical records are coded with exposures, whether the physician understands the nature of exposures and the potential health risks, there might be some education, a way to monitor quality of care for veterans, virtual library of good quality patient information, help educate patients about their condition, and give people a means to write medical reports onto their own personal CD.

Dr. Benjamin Natelson, Chair

I was hoping that in the intolerances, we would get those design issues in that we talked about.

Mr. Anthony Hardie

First, I think that at some point this has to be pulled into one document. On the Macro section, a couple of points. In short-term, its very important that we keep in throughout there, VA Persian Gulf War coordinators. We say, VA healthcare professionals, but I made the point yesterday, it's very important that we make it mandatory that those people are involved in every step of the process. Further down, in paragraph two, which is long-term, I'm concerned about the language "can." Say "The research *should* address" instead of "The research *can* address." And then later on, use something stronger than "may include."

Further down, there's a list of ideas – directing interested veterans to treatment trials. It's very important to make all veterans aware of treatment. [Group agrees to change it to "Advising veterans of available clinical treatment trials."]. The bit in there about the self-help guides . . . [Group agrees to revise to: "All veterans would receive either standard self-help care literature, or literature tailored to their specific needs."].

CDR David Seipel

Right now we're running out of time. We're tweaking this, and the sense of the group back here is, if we don't get this done right now, as soon as we go to present this to the group, whatever we present is in stone.

Dr. Benjamin Natelson, Chair

I can't believe it. Let me just say, there's just no way we can be railroaded.

CDR David Seipel

That's not what I'm trying to say. We've got people coming up to the microphone saying, "Lets wordsmith this, let's bold this word." We're trying to get through this too fast. We've got people back here trying to railroad the board into, "I need to have this specific word," "I demand . . ." That's not what we're here for. And I'm looking at it from an active duty standpoint. That's a great document, but you haven't said a thing about active duty and getting them involved in trial care. It's more than just VA. What I propose is, continue where we're going, give us a printout, there's people that would stay back for tweaking, while other presentations are being done.

Dr. Benjamin Natelson, Chair

Absolutely. There's just no way that we are done with this. What we are working in is within a time constraint to get something together, but this is not finished. What we've got here is sort of the skeleton and we've started putting some flesh on it, but there's a lot of details and tweaking, but let's tweak away. (Discussion continues, amongst the panel members, about how to complete the work at hand in the time available. People were already beginning to leave the room, and the panel members were having a conversation regarding what they would present).

LTC Charles Engel

I was focusing on what I was doing here and a question was asked about Section 3, routine primary care and collaborative primary care and how that is different. First of all, it's different because it's built into an overall approach. Currently, the way primary care is built in the VA and most healthcare systems, quite frankly, is it's whenever you feel like you have a difficulty, you come in and get care. Nobody talks to you if you don't come in and get care. This approach would involve a needs assessment that drives an assignment into a practice team panel, and the practice team panel would have responsibility for your care. Currently, if you go to a different clinic, you see a different physician. They have no idea who you are, they're starting from scratch. In this plan, you would have a practice team who would be responsible for on-going assessment of your health needs, and not only medication strategies, which is typically what you get in the context of a 15-minute visit, but other strategies that could be used to improve your health.

Mr. Anthony Hardie

I guess the concern that I have -- Madison, Wisconsin has already implemented this, if I'm not mistaken. It's sort of a cutting-edge approach, from what I understand, but they're trying it as a model for other VAs. The concern that I have is, it doesn't help me to be seen by a sociologist. It helps me to manage my daily life, but I'm getting worse, I'm not getting better. There's no mechanism built into here to report this research back. Congress has found over and over that the VA studies, the Gulf War registries, are not designed to do much of anything. They're not adequately built as a research program, they don't really assess anything. They're a collection of data, but it's not manageable. You can't compare across veterans. There's no reporting mechanism here. I really think it's important that we have some sort of reporting mechanism. It goes back to that essential team, I forgot what Joe called it, but whatever the central team is, there's a continual flow of information. Here we've got veterans that are not being able to be treated, we're trying to manage their care as best we can, but here are the symptoms that are not being treated, and pass that back up so somebody knows about this so they can be doing something about it. We need to incorporate that into this, somehow.

LTC Charles Engel

So what you would like is that information, based on these assessments, in the aggregate, would be provided to the macro level?

Dr. Nancy Fiedler

That was our intent.

Mr. Anthony Hardie

I believe it was your intent, but I don't believe it's in there.

Dr. Benjamin Natelson, Chair

I and you feel the pressure of time, but that does not mean that we're done. Actually, we got a stupendous amount of work done. Last comment.

Mr. Kirt Love

For me, when I go back to Texas, there isn't this room, there aren't these people all collectively together. I go back to Texas isolated again. So it is important to get as much of this done here, as possible.

[Group voices concerns about work that still needs to be done. The consensus is to bring it up in the general session].

Dr. Benjamin Natelson, Chair

The point is that most of us are out of here today, but we are not done.

Ms. Denise Nichols

There's a couple of things that were not mentioned in pharmacological and treatments that we might want to call in for experts to come in and be looked at, and that would be hyperbaric oxygenation, plasmapheresis that saved one of our Colonel's life, family support items. Nowhere did we talk about immune system drugs to help the immune system, we need to do something with the immune system. And there's two other real big things that are happening that we haven't brought up – our teeth are falling apart and our vision is going, and we need help with that and in the VA system, you can't get help until you get 100%. Would you like a minority report?

Dr. Anne Solomon

No, I think those are excellent suggestions and I think they should be, you'll get the copy and if

you have ten people, you just put it right in there.

The session was adjourned.

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